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GOVERNMENT'S OBLIGATION IN INDUSTRIAL HEALTH*

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WE MEET today at a time of revolutionary changes. In the field of industrial health, as elsewhere, the changing conditions are giving rise to new problems, which we must be prepared to face. First there are the changes in the composition of the labor forces. Older men, women, the physically handicapped and, in some industries, veritable youngsters are all going to work. The chairman of the War Manpower Commission has mentioned a working army of upward of 60,000,000. As we approach this number, we must leave out men of Class 1-*A* or 1-*B* selectee qualifications. There is a distinct probability that we must also leave out the eighteen- and nineteen-year-old boys. These workers, steadily increasing and without the physical adaptation and experienced work-habits of the men who have been called into service, are laboring harder and for longer hours than heretofore. Eight federal agencies — the Maritime Commission, the War Manpower Commission, the War Production Board, the Department of Commerce, the Department of Labor, the War Department, the Navy Department and the Public Health Service — have jointly subscribed to a policy of urging a forty-eight-hour week limit in war plants. This policy is in line with a statement issued by the Public Health Service nine months ago pointing out that industries operating on a twenty-four-hour-a-day basis must take special precautionary measures to minimize the effects of night work and the rotating shift.

Another important change has been brought about by the growth of boom-town conditions in many areas. The three basic essentials of public health — safe water, safe food supplies and proper sewage disposal — are jeopardized, especially in the more recent industrial and military mobilization areas. Add to this the problems of crowded clinics and hospitals, crowded housing and crowded transportation, and we have a situation that calls for the best services that our federal, state and local health authorities in combination have to give.

Perhaps the fastest and biggest changes have taken place in our factories. New processes, new machinery, new materials are now in use. Often they have been introduced too rapidly to receive the benefit of investigation from the standpoint of their effect on health. Of course, many of the health hazards are already too well known to call for further research. Welding, dermatosis-producing materials, siliceous dusts, benzol — these four potential occupational hazards come quickly to mind as examples of processes and substances whose dangers we have known for some time. But this easily available scientific knowledge has not been applied in our factories as completely as possible. There is only one way to bridge the gap between knowledge and application. That is by employing trained personnel to do the job. An insufficient supply of trained personnel is one of the great difficulties we have to face in industrial health conservation. Today there are approximately five hundred professionals and technicians in this country trained in the particular complexities of industrial hygiene. Five or six years ago there was hardly one fifth of the present number. Fortunately, the Public Health Service recognized the need at that time. We believed that it was our responsibility to help meet it and to stimulate similar preparation by industry, medicine and professional and technical schools. Each year since 1936 our Division of Industrial Hygiene has run orientation courses for in-service and field training. Without this preliminary start it is doubtful whether we could have handled the sharp upswing of demands for industrial-hygiene services — demands that were motivated largely by the conditions I have just described.

The first big job of the Public Health Service is that of directly assisting the War Department. The Division of Industrial Hygiene has completed surveys of eighty of the one hundred and fifty gov-

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ernment plants certified to us by the War Department to date. These key war plants include arsenals and airplane and munitions plants. In addition to military personnel, they employ several hundred thousand civilians. Our field and research services to the War Department are being continued and accelerated.

Our second job is to aid the forty-four state and local industrial-hygiene units, which are now operating in thirty-eight states. These units have co-operated with us by going all-out in their services to war industries. During the last fiscal year they investigated about seven thousand plants, and made recommendations covering nearly two million workers. As the war-production value of their services becomes better known to their fellow citizens as well as in Washington, I am sure that these states will intensify and speed up their investigations. We, in turn, co-operate with the states through the loan of personnel and scientific equipment, as well as in the continuation of our previous services. These services range all the way from making analyses of specimens as needed by the states to assistance in promoting a workers' health-education program. Since July, 1941, representatives of the Division of Industrial Hygiene have crisscrossed the country. They have visited almost every state to get firsthand information on industrial-hygiene problems in important war industries. On the basis of such information, they have appraised the states' facilities available to solve state problems, as well as determining to what extent the Division of Industrial Hygiene could augment personnel and equipment. The activities of the present forty-four state and local industrial-hygiene units are budgeted, during the current fiscal year, to the sum of approximately $1,250,000. The number of state and local personnel, despite many difficulties, has risen during the past year from about two hundred to the present figure of about three hundred and fifty.

The Division of Industrial Hygiene has recognized its obligation in blazing the trail in the recruitment and training of personnel. It has trained nearly one hundred men, fifty of whom are now on duty on a loan basis in twenty-eight states and under the Tennessee Valley Authority. Recently we conducted a two-week course in occupational dermatitis, which was attended by twenty-two leading physicians from every part of the country. The formal lectures were followed by visits to various war plants. We believe that when these doctors return home, they will be better equipped — not only to help themselves, but also to pass along some of the experience they have gained. Since more time is lost from work because of occupational dermatitis than because of any other occupational disease, we are certain that our course is a big step in the right direction.

Perhaps the longest-standing activity of the Division of Industrial Hygiene is its research program. In our laboratories today dozens of technicians are carrying on a hundred projects, almost every one of which bears directly on the war. These men are developing instruments for the detection and measurement of toxic dusts, fumes and gases. They are examining the relation between fatigue and different hours and types of work. Other men are doing confidential work in aviation medicine in collaboration with the Navy Department. With the greatly increased use of toxic substances in war production, some of our most immediately applicable work is in the study of the toxicity of explosives and solvents, airplane and armament metals, plastics and, last but not least, synthetic rubbers. These facts and figures are constantly being added to the reservoirs of industrial-hygiene "know-how" that we have gathered over the past generation — a reservoir that can be tapped by anyone who asks for aid.

Perhaps the most far-reaching obligation of the Public Health Service is to co-ordinate the health-conservation activities of industry, labor, medicine and interested government agencies. To this end we are co-operating with the War Production Board, which has already organized some sixteen hundred labor-management production-drive committees throughout the length and breadth of the Nation. We have prepared a comprehensive yet simple outline of a practical industrial-hygiene program, which has been placed in the hands of thousands of labor-management spokesmen to guide them in this work. There is as great a need for co-ordinated activity in this field as there is among our air, land and sea forces. Each member of our working army is more than a person exposed to a range of hazards within the factory gates. When the whistle blows at the end of the day he becomes a citizen of his community again — a citizen with a family, friends and social obligations. It is this total man, whom industrial hygiene and all interested groups must consider. One should recall, for example, that although sickness, accidents and deaths due to hazards on the job may be impressive, these account for less than 10 per cent of the industrial time loss. The remaining 90 per cent or more of lost time is due to disabling nonoccupational diseases. In other words, nine out of ten workers who are off the job and in the hospital or sickroom are there because of some general illness. The respiratory diseases, digestive disorders and certain chronic diseases take a greater toll of American life and effort than the worst pounding Hitler's *Luftwaffe* gave Britain after Dunkirk. Our

tactics, then, must be to attack the problems of disease from two sides in a combined assault — in the community as well as in the factory.

The venereal-disease clinic, the nursing service, the dental service, the public-health education service, the sanitation section, the maternal and child-health service must reach the industrial worker and his family to a far greater extent than mere routine functions permit. The industrial-hygiene unit has a close, informed relation with management and employees, and therefore is the logical co-operative channel through which these services can reach the worker. The local health department, correspondingly, is the channel through which industrial hygiene can be brought to bear directly on the health problems of workers in small plants. The health officer has at his command the state industrial hygienists, who are trained and equipped to co-operate with him, just as he, by virtue of his position, has the most complete acquaintance with local needs and resources. In this sense, therefore, every division of a state or local health department should play a part in building the foundation for promoting the health of workers. If we agree on the changing nature and extent of our common problems, I think we shall agree that we must prepare for the possibility of changing our methods of dealing with them. As the ratio of physicians to population becomes dangerously low in many areas, we must consider the possibility of industrial doctors' leaving their dispensaries for certain periods of community practice. If a skilled man is off the job in order to care for his sick wife, it is common sense (as well as enlightened humanitarianism) to treat the woman so that the man can return to war work, where every pair of hands is needed. It would seem that the day is coming when, in many areas, the community physician's practice and the plant physician's patients will have to be handled by one and the same man. That man should have — and must have — the co-operation of every governmental agency. He should have — and must have — the understanding and backing of his medical society. He must have the co-operation of the war-production-drive labor-management committees. He must have the same respect, encouragement and attention that top management already gives to operations departments. Last and not least, he must have the friendship and understanding of the workers whom he treats, for only they, in the final analysis, can apply to their daily lives the precepts that he teaches.

All of us, no matter in what field we work, have a single star to steer by. That is the belief that every man and every woman saved from illness or accident is a skill saved as well as a person saved. In the months ahead we shall need every skill, for it is only the total of our many skills on the home front and the battle front that will hasten the final victory. In a changing world, our determination to overcome any and all obstacles through constant effort and teamwork must remain changeless.

THE DIAGNOSIS OF SPRUE IN NONTROPICAL AREAS*

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SPRUE and spruelike states are not rare in northern latitudes, but the complicating features are often so prominent that the underlying disorder is not immediately recognized. Four patients seen within the last two years at the Massachusetts Memorial Hospitals illustrate not only the wide variety of symptoms encountered but also the ensuing diagnostic difficulties. In each of these cases initial failure to make the correct diagnosis postponed adequate therapy, which, in sprue, may not be completely curative but will often allow a severely debilitated person to resume a normal life. Hence reports of these patients are presented, not as complete case reports of sprue seen in nontropical areas, but in order to emphasize the secondary phenomena that may be encountered. Excellent descriptions of nontropical and tropical sprue, as well as complete case reports, can be found in the writings of Thaysen,[1] Snell,[2] Miller and Barker[3] and Kantor.[4]

Spruelike states are characterized by steatorrhea, which apparently is not the result of pancreatic disease. Under this heading, tropical sprue, nontropical sprue (idiopathic steatorrhea) and celiac disease of children may be listed. Whether these conditions represent different aspects of the same disease is still a matter of dispute,[1, 2] but for the present purposes, the two adult forms will be considered under the single heading of sprue.

The outstanding feature of this disorder is an excess output of fecal fat, which has led to the conception that the basic abnormality of sprue is a malabsorption of lipids. It is more likely, however, that patients with this disease absorb all substances poorly, even water and gases; and absorption tests using glucose[5] and glycine[6] substantiate this conception with respect to sugars and amino acids. On the other hand, the small intestine of man is long enough to compensate for the delayed absorption rate of glucose and amino acids; hence these substances do not appear in the feces to excess. Fats, however, are much more slowly absorbed, even by the normal bowel, and a delayed lipid absorption then causes fatty substances to be spilled into the colon. This, in turn, leads to the fatty stools of sprue. Patients who have had extensive granulomatous disease, resections or short circuit of the small intestine may also have steatorrhea,[7] but in these cases the curtailment of the absorbing surface rather than a generalized defect predisposes to the spruelike state. It is then clear that the symptoms of sprue may be predominantly related to the gastrointestinal tract and its disturbed functions; or these symptoms may be minimal, and the patient's major complaint will then be the result of a dietary deficiency conditioned by the poor absorptive capacity of the bowel. Naturally, a deficiency of fatty substances is most likely to occur.

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STOOLS

Typically, the patient with sprue has frequent bowel movements consisting of soft, light-yellow, frothy and greasy fecal material. Actually none of the four patients consistently had stools fitting this description during the period that each was under observation, and two never passed stools of this character.

Patient H. S., an unmarried woman, thirty-one years old, of Syrian extraction, complained of gross hematuria of two days' duration. Because she gave the additional history of increasing fatigue, weight loss and hoarseness, the diagnosis of adrenal, laryngeal and renal tuberculosis was entertained. Only on direct questioning did the patient state that she had had an increasing frequency of bowel movements for two or three months. In the hospital, the movements were watery and dark brownish green. The high lipid content of these stools was grossly apparent only after they had been allowed to stand for several hours, when a thick layer of fatty material gradually accumulated on the surface.

Patient W. J., a man of forty-seven, who had been known to suffer from hypocalcemic tetany and from a macrocytic anemia moderately resistant to liver-extract therapy for four years, moved his bowels once daily and occasionally took mineral oil for constipation. Though he had no diarrhea, his stools were light and somewhat greasy in appearance. Sprue had not been considered in his case because of the formed character of the feces.

Patient W. C., a man of thirty-six, had the typical stools of sprue on admission, but after four months of treatment, bowel movements occurred only twice daily, one movement being formed, the other watery. Although the fat intake was limited to 25 gm. daily, the stools continued to be light yellow,

suggesting that this color is not necessarily produced by a high percentage of fecal fat.

Fat-balance studies on all three patients showed that they excreted 42, 25 and about 80 per cent* of their dietary fat, respectively (normally less than 10 per cent is excreted). But it is not necessary to do such laborious studies; in each of these cases, a microscopic study of a fecal specimen stained with sudan III was enough to show the abnormal steatorrhea.

The stools of all these patients were cultured, but no pathogenic intestinal bacteria were identified. A heavy growth of Parasaccharomyces A (*Monilia albicans*)[8] was, however, obtained from both the feces and the small-bowel contents of patient W. C. When the patient improved clinically, the parasaccharomyces disappeared from the stools, only to reappear when a mild relapse was precipitated by his failure to observe the prescribed dietary and therapeutic regimen. These observations are in accord with the now generally accepted belief that parasaccharomyces are secondary invaders, not etiologic agents, in sprue.

TABLE 1. *Results of Significant Laboratory Studies When the Diagnosis of Sprue Was First Made.*†

PATIENT	HEMATOLOGIC STUDIES							SERUM		PROTHROMBIN VALUES
	RED-CELL COUNT	HEMOGLOBIN	HEMATOCRIT	M.C.V.	M.C.H.	M.C.H.C.	WHITE-CELL COUNT	CALCIUM	PHOSPHORUS	
	$\times 10^6$	% *normal (15.6 gm.)*	%	*cu. μ*	*γγ*	%	$\times 10^3$	*mg./100 cc.*	*mg./100 cc.*	% *normal*
W. C.	2.92	70	34.8	119	37.3	31.3	5.0	8.0	2.0	30
W. J.	3.11	66	33.8	109	32.8	30.2	8.0	7.3	2.7	60
H. S.	2.56	42					18.0	6.1	1.6	19
J. M.	2.09	33					7.3	5.4	1.6	10

†Patients H. S. and J. M. were experiencing active tetany and had purpuric manifestations.

DISTENTION AND CRAMPS

A well-known symptom of sprue is abdominal distention, the result of abnormal accumulations of gas and liquids in the loops of the small and the large bowel. This distention has usually been ascribed to intestinal fermentation, but a better explanation can be found in the marked loss of intestinal tone, which prevents proper propulsion, elimination and absorption of gases. As in the distended bowel behind a partial obstruction, however, deep contraction waves may pass over the distended loops, producing typical abdominal colic. Usually the atonic symptoms greatly exceed those due to the hyperperistalsis, but not always. The combination of atony with occasional hyperperistalsis leads to the unusual intestinal pattern that roengenologic studies have demonstrated in sprue.[9-11]

Patient W. C. had had intermittent bouts of progressively severe diarrhea for fifteen years. With the diarrhea, he suffered from abdominal distention and cramps. Eight months before admission to the hospital, he was awakened at night with particularly severe colic and distention, accompanied by some nausea and vomiting. An emergency operation for intestinal obstruction was done, but the laparotomy revealed no local lesions, merely a generally loose and flabby bowel stained diffusely with a brown pigment (hemofuscin). Nevertheless, an ileostomy was done. Since symptoms suggesting intestinal obstruction persisted, two more ileostomies were performed in a six-month period, each ileostomy being placed higher than the previous one, and each being unsuccessful in alleviating the symptoms. Treatment of the sprue, after the diagnosis was finally made, relieved the symptoms promptly. In spite of all measures, however, this relief was not permanent. Occasional cramps and hyperperistalsis occurred, but the negative findings at previous operations, as well as careful diagnostic studies with the Miller–Abbott tube, ruled out organic obstruction. An examination of this patient's stool before the first ileostomy would have pointed to the correct diagnosis, and a combined diagnostic and therapeutic use of the Miller–Abbott tube[12-14] would have shown that the motor disorder was generalized, not local.

ANEMIA

The anemia that attends sprue may simulate that of pernicious anemia or may be hypochromic and microcytic.[15] In these four patients, the variable hematologic characteristics of this disease are well illustrated in that two had microcytic and two macrocytic anemia (Table 1). The picture was complicated in patients H. S. and J. M., however, since both suffered from purpura and had lost considerable blood at the time the diagnosis of sprue was first established.

When the mean corpuscular volume and the mean corpuscular hemoglobin are increased over their normal upper limits (92 cubic microns and 31 gamma gamma respectively), as was the case in patients W. C. and W. J., the differential diagnosis between sprue and pernicious anemia may

*This patient had an ileostomy; hence, an exact quantitative collection of the ileal contents was impossible.

present some difficulties. As a matter of fact patient W. J. had been considered to have Addisonian anemia three years previously, because he had a red-cell count of 2,240,000, a hemoglobin of 55 per cent and gastric achlorhydria. This diagnosis, however, failed to explain the other findings — the disproportionally large abdomen, the attacks of hypocalcemic tetany and the rather disappointing response to therapy with parenteral liver extract. Usually one can expect that a potent preparation of liver will produce a dramatic response in pernicious anemia, particularly if the anemia is severe. In patients with sprue, liver extract also benefits the anemia, but the amount necessary for this result is often two or three times that needed in pernicious anemia, and a complete eradication is difficult to achieve.

Tetany

Each of the four patients had tetany at one or more periods during his or her illness. Usually the carpopedal spasms were recognized for what they were, but in one case (patient W. C.) a physician who failed to recognize that he was eliciting a Trousseau sign chided the patient when the inflation of the sphygmomanometer cuff around the arm produced a painful spasm of the hand and fingers. Even when Chvostek and Trousseau signs were not obtainable, the serum-calcium levels were below normal (Table 1).

Formerly this hypocalcemia was ascribed to the formation of insoluble calcium soaps in the intestine. Studies of the intestinal tract in man show, however, that the pH of the small bowel rarely rises above 7.5,[16, 17] and in a medium with a pH of less than 8.0 many soaps do not form.[18] Hence the suggestion of Albright and Stewart[7] that faulty calcium absorption is a secondary result of poor absorption of the fatty vitamin D offers a more reasonable explanation of the hypocalcemia. Thus, for instance, massive therapy with vitamin D will raise the serum-calcium level in patients with steatorrhea.[19] On the other hand, increasing the dietary fat in patients with sprue is followed by an increased output of fecal calcium.[20] These facts suggest that both mechanisms may play a part in producing hypocalcemia.

In spite of the low serum-calcium content, none of our patients showed definite osteoporosis of the long bones. The serum-phosphatase levels were normal.

These observations suggest that sprue should be suspected, as well as hypoparathyroidism and advanced renal disease, when evidences of hypocalcemia are found.

Bleeding Tendency

Patient H. S., as already mentioned, entered the hospital with a chief complaint of hematuria, which was ascribed to a tuberculous renal lesion. Three days after the beginning of the hematuria, the patient commenced to bleed from the nose and mouth as well, and huge purpuric areas formed all over the body (Fig. 1). Only then was the correct diagnosis suspected. The prothrombin time had dropped to 1 per cent of normal. Patient J. M.* similarly developed massive purpuric areas within the course of two days, although he had had gastrointestinal symptoms for four years previously. Table 1 gives the prothrombin values in the series.

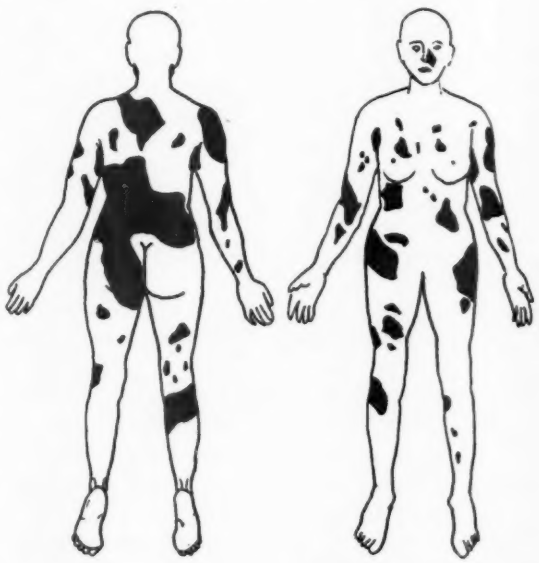

Figure 1. *Distribution of Subcutaneous Hemorrhages in Patient H. S.*

The cause of the prothrombin deficiency is in all probability the same as that of the hypocalcemia, namely, the failure to absorb a fat-soluble vitamin — in this instance vitamin K. Parenteral injection of the fatty vitamin or oral administration of a water-soluble preparation will immediately arrest the bleeding tendency in these cases. If the diagnosis is not correctly made, the patients may die of internal and external hemorrhages.

Vitamin A Deficiency

The symptoms of vitamin A deficiency are less dramatic than those of vitamin D or K deficiency, and therefore are often not apparent unless specifically investigated. Two of the patients complained of night blindness, but biophotometer measurements were not carried out. Gross xeroph-

*This case has been reported in detail by Kark, Souter and Hayward.[21]

thalmia was not present. One patient had a dry, scaly skin, but in the presence of an associated deficiency of the vitamin B complex, the significance of this lesion was equivocal. On the other hand, the content of Vitamin A and its precursor, carotene, in the blood can be determined with considerable accuracy.[22] Figure 2 shows that the

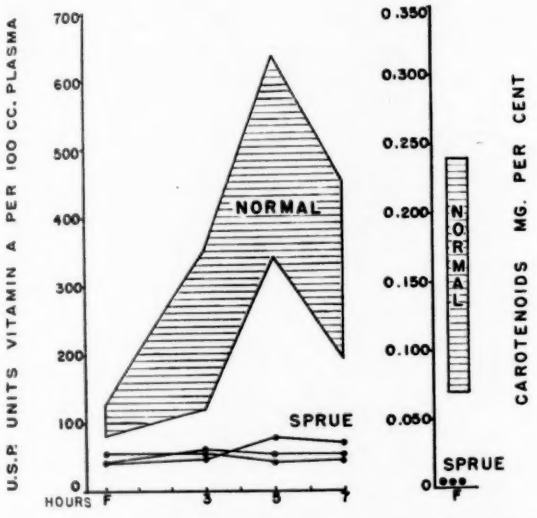

FIGURE 2. *Vitamin A Absorption Test and Carotenoid Level in Sprue.*

The values in sprue (solid lines and dots) are compared with those in normal persons (shaded area). The fasting figures are indicated at F. *The scale on the right shows the fasting carotenoid levels in patients with sprue (three solid dots) and in normal persons (shaded area).*

fasting levels of vitamin A in the plasma were strikingly decreased in the 3 patients in whom this determination was carried out, and that carotene was to all intents and purposes completely absent. Furthermore, after a large dose (250,000 international units) of vitamin A was given by mouth, little absorption occurred so far as could be told from the plasma levels. Low vitamin A levels in the plasma and flat absorption curves may, however, be found in other diseases (infections[23, 24] and hepatic disorders[25]), and do not necessarily indicate impaired absorption[26]; but the very low carotene values are particularly significant in establishing the diagnosis of steatorrhea.

Vitamin B-Complex Deficiency

Patients with tropical sprue often have striking evidence of deficiency of the vitamin B complex, especially of nicotinic acid and riboflavin deficiency. Patient W. C., who had had sprue for fifteen years, was the only one of the patients who exhibited these signs. Cheilosis, angular stomatitis and a dark-red and smooth tongue were prominent. Also striking was the deep, fiery-red color of the mucosa of the proximal and distal portions of the ileum at the site of the ileostomy. Oral administration of 9 mg. of thiamin hydrochloride, 300 mg. of nicotinic acid, 5 mg. of riboflavin and six tablets of Brewer's yeast daily had no apparent effect on the oral and mucosal changes. When thiamine hydrochloride was given parenterally (10 mg. three times a day intramuscularly), an acute exacerbation of the stomatitis occurred. Within one week, the tongue became purple, multiple aphthous ulcers appeared, and the patient had to be given anesthetic mouthwashes for relief. Thereupon he was given parenterally a preparation of vitamin B complex said to contain 3 mg. of thiamine hydrochloride, 10 mg. of nicotinic acid amide, 0.5 mg. of riboflavin, 0.45 mg. of pyridoxine and 1.68 mg. of pantothenic acid per cubic centimeter. He received 2.5 cc. of this preparation daily as well as 2.5 cc. of a crude liver extract (1 unit per cubic centimeter). In three days the symptoms disappeared; one week later the tongue was pale and the fissures at the corner of the mouth had healed; and in one month the lingual papillae began to grow. During this time, the mucosa of the ileum became pinker and much less irritated in appearance.

These observations suggest that this patient was unable to absorb the vitamin B fractions which he was given by mouth, or that the oral doses contained insufficient quantities of the necessary materials. Since the oral doses were given over a period of two months, it is more than likely that the buccal and lingual lesions would have responded had this patient's absorption of riboflavin and nicotinic acid been adequate.

The other three patients had no gross evidence of impaired absorption of the vitamin B complex. This difference was probably quantitative, not qualitative; that is, patient W. C. had by far the greatest absorption defect in respect to all substances and had suffered from this defect for the longest period of time.

Clubbed Fingers

Manson-Bahr[27] mentions clubbing of the fingers as an occasional finding in nontropical sprue. Patient W. J. exhibited these digital changes. Since this sign has also been observed in patients with ulcerative colitis,[28] it appears that chronic malfunction of the intestine may be considered as one of the causes of clubbed fingers.

Summary and Conclusions

When sprue and spruelike states are encountered in nontropical areas, the classic features of tropical sprue may be absent or may be obscured

by the secondary nutritional disturbances of the disease. On the basis of observations made on four cases, it appears that the stools are not always numerous or greasy on gross inspection. The disorganized motor activity of the intestines may occasionally produce symptoms suggesting organic intestinal obstruction. In other patients, the gastrointestinal symptoms play a secondary role in the clinical picture, which may be featured by tetany, a generalized bleeding tendency or anemia. Vitamin A and particularly carotene are present in low concentrations in the plasma, and night blindness is at times noticed. Evidences of a deficiency of the vitamin B complex, such as stomatitis and glossitis, are not always found, especially in the nontropical variety of sprue. Occasionally digital clubbing is observed.

The diagnosis of sprue in these four cases was made respectively eight months, three years, four years and fifteen years after the onset of symptoms. This delay may be ascribed to the facts that this diagnosis is not considered in northern climates and that the typical picture of sprue may be obscured by such features as have been described. The diagnosis, once thought of, is not difficult to make, a simple sudan III stain of the feces usually being sufficient to determine the presence of steatorrhea. To establish the diagnosis completely, determinations of prothrombin, calcium and carotene in the plasma, roentgenologic studies of the small intestine and, possibly, pancreatic function tests may be necessary. In most cases, however, the clinical picture combining the characteristics of a chronic but noninflammatory intestinal disorder with anemia and evidences of deficiencies of vitamins A, D and K should be sufficient to bring the diagnosis of sprue to mind.

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THE TREATMENT OF ANGINA PECTORIS WITH TESTOSTERONE PROPIONATE*

Further Observations

MAURICE A. LESSER, M.D.†

BOSTON

IN a previous communication,[1] the favorable effect of testosterone propionate in patients with the syndrome of angina pectoris was reported. In that study, 24 patients — 20 men and 4 women — ranging in age from forty to seventy-seven years, with an established diagnosis of angina pectoris were given periodic injections of testosterone propionate. The drug was administered every second to fifth day in 25-mg. doses for a total of five to twenty-five injections, with an average of eleven injections. The frequency, severity and duration of attacks were diminished, and all patients were able to increase their physical activity considerably without precipitating an attack of pain. No improvement was noted in patients following control injections of plain sesame oil, although in these control patients testosterone propionate therapy subsequently did have a favorable effect. No untoward effects from the use of this drug were noted, and its beneficial effects continued from two to twelve months after treatment was withdrawn. Similar results have been obtained by other investigators.[2-4] In the majority of cases there was a general lowering of blood-pressure levels during the course of testosterone propionate therapy. In view of these favorable results, further studies have been conducted to obtain accurate measurements of the effect of testosterone propionate therapy in patients afflicted with angina pectoris.

METHOD

Twenty-two patients with angina pectoris — 21 men and 1 woman — were given testosterone propionate‡ therapy, with results similar to those previously reported,[1] making a total of 46 patients successfully treated.

Of this group, 4 patients were studied by means of exercise-tolerance tests before and during the course of therapy, to obtain quantitative measurements of their improvement. The patients were subjected to the two-step test designed and described by Master and Oppenheimer.[5] Each patient ascended on one side of the steps and descended on the opposite side, then turned and repeated the procedure. One ascent and one descent constituted one trip. Each patient exercised until an anginal attack was precipitated. The number of trips made before the attack developed was recorded by one observer and the duration of the attack was clocked by another. Each patient was tested several times prior to the institution of testosterone treatment in order to obtain a base line for comparison, and was tested periodically during the course of the therapy. The exercise-tolerance tests were performed under standardized conditions — approximately two hours after meals, at a fairly constant rate of speed, and at a room temperature of 72(±4)°F.

RESULTS

The results obtained are summarized in Table 1. Fuller details are presented in the case histories. In each of these patients it was found that the amount of work done before the development of an anginal attack was increased under testosterone therapy and that the severity of the attacks, as measured by the duration of the pain, was correspondingly diminished. In each case subjective improvement was reported before quantitative changes could be demonstrated.

CASE REPORTS

CASE 1. E. W., a 57-year-old grocery clerk, had a history of angina pectoris of 6 months' duration, during which time he was unable to perform his duties. The pain was substernal in location and was relieved by rest or nitroglycerin.

Physical examination revealed a blood pressure of 140/80. The heart was not enlarged, there were no murmurs or thrills, and the rate and rhythm were normal. The heart sounds were poor in quality. The electrocardiogram and sedimentation rate were within normal limits.

The exercise-tolerance tests prior to testosterone propionate therapy ranged from 35 to 42 trips, and the duration of the substernal pain varied from 155 to 178 seconds. Definite improvement was reported by the patient after the third injection. Quantitative improvement, however, did not occur until after the sixth injection, and after the sixteenth injection he was able to double his exercise before precipitating an attack. During this period the severity of the attacks was likewise decreased as measured by the duration of the pain, which fell from a maximum of 178 seconds to 55 seconds (Fig. 1). Following the twelfth injection the patient returned to work, and has suffered no further attacks.

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‡Kindly supplied by Ciba Pharmaceutical Products, Incorporated, Summit, New Jersey, under the trade name of Perandren.

Case 2. W. W., a 64-year-old physician, had a history of angina pectoris of 4 years' duration. The pain was brought on by climbing one flight of stairs or walking three or four city blocks, and was relieved by rest or nitroglycerin. He required 2 to 4 nitroglycerin tablets before precipitating an attack and the pain lasted only 23 seconds (Fig. 2).

Case 3. B. M., a 54-year-old boilermaker, had a history of angina pectoris of 9 months' duration that became

Table 1. *Results of Exercise-Tolerance Tests in 4 Patients Treated with Testosterone Propionate (25 mg. per dose).*

Patient	No. of Injections		Time		Total No. of Injections	Duration of Therapy	No. of Trips*		Duration of Pain†	
	Before subjective improvement	Before quantitative improvement	Before subjective improvement	Before quantitative improvement			Before therapy	After therapy	Before therapy	After therapy
			days	*days*		*days*			*sec.*	*sec.*
E. W.	3	6	14	26	16	87	39	82	169	55
W. W.	3	8	14	32	12	57	39	71	92	38
B. M.	2	6	5	33	10	78	43	76	45	24
J. W.	4	6	14	21	14	63	27	47	72	46

*Trips — average of three tests preceding inception and cessation of therapy.
†Pain — average of three tests preceding inception and cessation of therapy.

daily. The pain was substernal and radiated down the left arm.

Physical examination revealed a blood pressure of 140/70. The heart size was within normal limits, the sounds were fair in quality with a harsh systolic murmur at the base; no thrills were present. The electrocardiogram showed

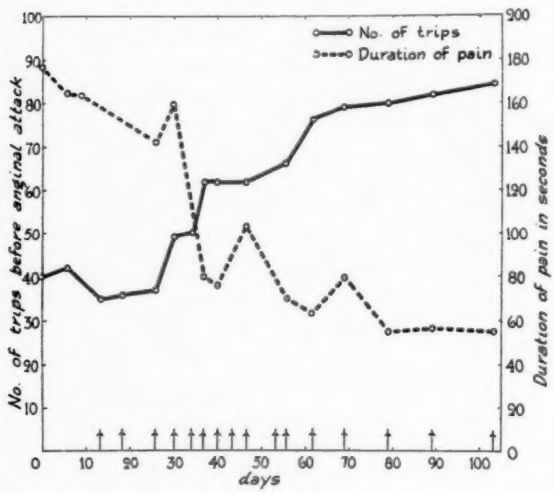

Figure 1. *Patient E. W.*

This and the other three charts (Figs. 2, 3 and 4) show the effects of testosterone propionate therapy on exercise tolerance and the duration of anginal pain. In each chart, an arrow represents one injection of 25 mg. of testosterone propionate.

a high degree of left-axis deviation, and frequent ventricular extrasystoles with runs of bigeminal rhythm. The patient was not taking digitalis.

After only three injections of testosterone propionate the patient reported that he was able to perform his usual duties without resort to nitroglycerin. The exercise-tolerance test, which prior to testosterone propionate therapy required from 32 to 43 trips to produce anginal pain lasting from 90 to 94 seconds, showed definite improvement after the eighth injection. At the end of twelve injections the patient was able to perform 72 trips

progressively worse; he had been unable to work for 4 months. The pain, which was substernal, was precipitated by the climbing of one flight of stairs or the ingestion of a heavy meal, and was relieved by rest or nitroglycerin.

Physical examination revealed a blood pressure of 100/75. The heart was not enlarged, and the rate and rhythm were normal. There were no thrills or murmurs, but the sounds were distant. An electrocardiogram showed a deep Q_3 and late inversion of T_3, suggesting an old posterior myocardial infarction.

The exercise-tolerance test prior to testosterone propionate therapy ranged from 39 to 47 trips and the duration of the pain varied from 35 to 60 seconds. Subjective

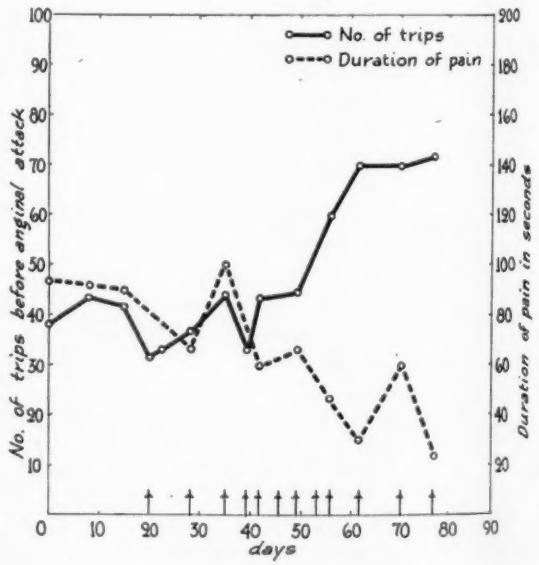

Figure 2. *Patient W. W.*

improvement was reported after the second injection. It was not until after the sixth injection, however, that quantitative improvement was observed. Then the patient was able to make 80 trips before precipitating an attack. The duration of the pain was decreased to as low as 15 seconds

during the period of treatment (Fig. 3). After the fifth injection the patient returned to his work on an 8-hour shift and experienced no further attacks.

Case 4. J. W., a 60-year-old barber, had a history of angina pectoris of 13 years' duration. Substernal pain

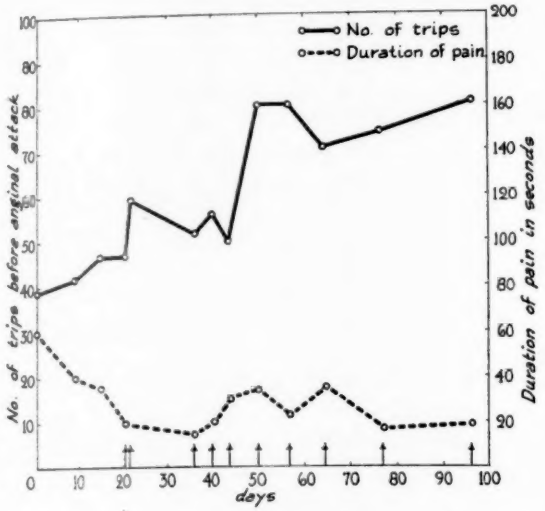

Figure 3. *Patient B. M.*

accompanied by numbness of the left hand was precipitated by climbing one flight of stairs or walking two city blocks, and was relieved by rest or nitroglycerin. He required 4 or 5 nitroglycerin tablets daily.

Physical examination revealed a blood pressure of 120/80. The heart was not enlarged, and the rate and rhythm

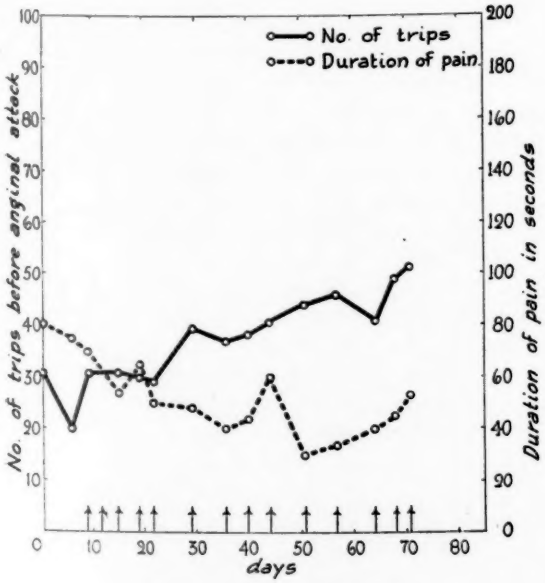

Figure 4. *Patient J. W.*

were normal. There were no thrills or murmurs, but the sounds were distant. An electrocardiogram showed a deep Q_3 and late inversion of T_3, suggesting an old posterior myocardial infarction.

The exercise-tolerance test prior to testosterone propionate therapy ranged from 20 to 31 trips and the duration of the pain from 70 to 80 seconds. Improvement was reported by the patient after the fourth injection, but it was not until after the sixth injection that quantitative improvement was observed. This reached its maximum after the fourteenth injection, when he was able to make 51 trips before experiencing substernal pain, which lasted 53 seconds. The shortest duration of pain after therapy was 30 seconds (Fig. 4). After the sixth injection the patient required only the occasional use of nitroglycerin.

Discussion

The present study provides further evidence of the value of testosterone propionate in the treatment of angina pectoris. This agent not only reduces the frequency of the attacks but decreases their severity when they do occur. It is important, however, to stress that it does not give immediate relief from an anginal attack, as does nitroglycerin. Furthermore, the improvement after the use of this drug varies with the individual patient both in time of onset and in degree. Whereas some patients in this series showed improvement after the second or third injection of testosterone propionate, there were others in whom no improvement was noted until the eighth, ninth or even tenth injection. Again, some patients required as many as fifteen to twenty-five injections over a period of months before therapy could be discontinued. These considerations emphasize the importance of individualizing each case and of giving an adequately long course of treatment. It seems doubtful whether giving the drug more frequently would produce more favorable results, since the time element plays such a significant role in obtaining the desired effect. This is borne out by the results obtained in the group of patients reported here. An average of twenty-eight days elapsed before quantitative improvement was noted, and a period of forty-three days elapsed before this improvement became marked. Although it is recognized that spontaneous improvement may occur in some patients with angina pectoris over the course of weeks or months, it would be most unusual for this improvement to occur uniformly in a large series of patients in such a short space of time.

Since the beginning of the present study, not enough time has elapsed to determine the duration of the beneficial effects of testosterone propionate therapy. In the previous study[1] it was noted that this period varied with the individual patient. The shortest period of benefit was two months, whereas the longest period that a patient has been free of anginal attacks is eighteen months. It is significant that those patients who returned for further treatment because of a recurrence of pain reported that their attacks were less severe than originally, and furthermore, it was found that fewer injec-

tions were required to control them. Of the 24 patients originally reported, 3 have required a second course of therapy and 1 a third.

Summary

Twenty-two patients with angina pectoris — 21 men and 1 woman — were given testosterone propionate therapy with results similar to those previously reported, making a total of 46 patients successfully treated.

Four patients were studied by means of exercise-tolerance tests before and during the course of therapy, to obtain quantitative measurements of their improvement.

In each of these patients the amount of exercise before the development of an anginal attack was markedly increased under testosterone therapy, and the severity of the attacks, as measured by the duration of the pain, was correspondingly diminished.

In each case, subjective improvement was reported before quantitative changes could be demonstrated by the test employed.

In the use of testosterone propionate for the treatment of angina pectoris, it is important to individualize each patient on the basis of his response to the drug and to give an adequately long course of treatment.

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MEDICAL PROGRESS

HEMATOLOGY (Concluded)*

William Dameshek, M.D.†

BOSTON

Normocytic Anemia with Leukopenia and Thrombocytopenia

IT SEEMS to be common practice nowadays in the therapy (and diagnosis) of a given case of anemia to give liver extract, iron and the vitamin B complex. If the patient fails to respond to this regimen, the diagnoses of pernicious anemia, chronic iron deficiency and B complex deficiency are considered doubtful and another diagnosis is considered. This method of treating anemia is to be deplored, because in the first place it does not take cognizance of the fact that anemia is not a disease but only a symptom, and in the second place it fails to advance the physician's knowledge regarding the value of specific remedies in the treatment of anemia. In short, it is not only unscientific but may be distinctly harmful to the patient, since such conditions as occult hemorrhage, malignancy and myxedema may be missed.

In a number of cases failing to respond to the above medications, the anemia is normochromic and normocytic (or perhaps somewhat macrocytic) and is associated with leukopenia and thrombocytopenia. Thus there is pancytopenia; that is, all the elements in the blood derived from the marrow are reduced. This type of blood picture often indicates some type of bone-marrow involvement: hypoplasia, aplasia, leukemia or neoplastic infiltration, fibrosis, failure of cellular delivery as in spleen disease, or failure of cellular maturation as in pernicious anemia.

When pancytopenia is present, the diagnosis of aplastic anemia is often made. Strictly speaking, this term should be reserved for cases in which the red bone marrow is actually hypocellular or acellular and almost completely occupied by fatty tissue. In a series of 26 cases in which bone-marrow biopsy was performed, Vaughan[54] found 12 with a remarkable reduction in marrow cellularity and predominance of fatty tissue. However, a number of cases showed either normal or increased cellularity. Similar findings in his own cases led Rhoads[55] to call the condition "refractory anemia," under which designation he grouped a variety of states with different bone-marrow findings but with refractoriness to therapy as an outstanding feature.

Although in Rhoads's earlier observations the state of the bone marrow was not seriously con-

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

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sidered, more recent articles by Bomford and Rhoads[56] present careful studies of this tissue. The term "refractory anemia" is in some respects unfortunate because it emphasizes refractoriness to therapy rather than the diverse etiologic and pathologic changes that are present. In my own experience, it is of distinct importance to determine the status of the marrow, the possibility of hepatic, splenic or thyroid disease, the presence or absence of a hemolytic process and the possibility of a disorder of fat metabolism, such as Gaucher's disease. Despite the reduction of red cells, white cells and platelets in the blood, the bone marrow at biopsy may be extremely cellular. Leukemia — myelogenous, lymphatic or monocytic — shows extreme leukocytic proliferation; lymphosarcoma and Hodgkin's disease may show the characteristic cellular proliferations of these diseases; and carcinoma may show neoplastic cells. Fibrosis, aplasia and so forth may be readily seen and Gaucher cells are quite easily recognized. From the standpoint of prognosis and possible therapy, it is important to discriminate between these conditions, and the sternal bone-marrow biopsy, whether performed by simple puncture — which is adequate in most cases — or by trephine, is preeminent in this regard. Myxedema should not be forgotten as a cause of refractory normocytic anemia, and I have seen a number of these cases treated for various blood conditions. Hepatic disease, particularly with splenomegaly, or various conditions in which splenomegaly is prominent — splenic-vein thrombosis, Gaucher's disease and even certain cases of hypersplenic hemolytic anemia — may result in pancytopenia. Splenectomy may be of definite value in such cases in restoring the blood picture to normal levels.

"Pancytopenia" is perhaps a better term than "refractory anemia" because it indicates simply that the cells in the blood are all reduced. In any event, one should realize that the finding of these hematologic abnormalities is merely a point of departure for further careful studies, which may include the marrow, the liver function, the basal metabolism, the urobilinogen excretion and so on. Pancytopenia, like anemia, is merely a symptom that requires clarification before a definite diagnosis can be determined.

The therapy of aplastic anemia, and in fact of most of the cases showing pancytopenia, — except those in which myxedema, splenic disease or increased hemolysis can be demonstrated, — is admittedly unsatisfactory. Vaughan[54] tried sternal bone-marrow transfusions in 4 cases of aplastic anemia with completely negative results. I have had similar experiences in both adult and juvenile aplastic anemia. Congenital hypoplastic anemia of infancy and childhood is a definite entity in which there is a congenital failure of erythropoiesis. These children may be kept alive and well indefinitely by repeated transfusions. Splenectomy is of questionable benefit, but may be valuable if there is any evidence whatever of increased blood destruction. Kohlbry[27] found no effect from sternal bone-marrow transfusion. The value of this procedure,[58] in which a few cubic centimeters of normal sternal marrow admixed with blood is placed in a patient's sternal-marrow cavity, must be seriously questioned.

Hemolytic Syndromes

Familial Types

A classification and a discussion of the mechanisms of the hemolytic syndromes were presented in last year's review.[59] In an American Medical Association exhibit, Dameshek, Greenwalt, Tat and Dreyfus presented in graphic form the physiologic, etiologic and clinical aspects of the various hemolytic syndromes, including the familial and acquired hemolytic anemias and the hemoglobinurias.* There are three types of familial, hereditary hemolytic anemias: spherocytic, Mediterranean target-oval-cell and (African) target-sickle-cell. The spherocytic type is familiar; ordinarily known as congenital hemolytic jaundice, it responds well to splenectomy. The Mediterranean target-oval-cell syndromes (commonest in Italians and Greeks) vary greatly in their severity from the fatal Cooley's anemia to mild hypochromic anemia with target and oval cells.[2, 60] One of their characteristic features is the presence of the target cell in increased numbers. Since these cells are thinner than normal, the hypotonic fragility test shows increased resistance. With the target cells are usually found varying numbers of oval or elliptical and heavily stippled erythrocytes. Despite the low color index, which is always present, these cases are completely refractory to iron therapy. They are important diagnostically since icterus, splenomegaly, anemia, stippling of the red cells and even heart murmurs are common. From the hereditary standpoint, they are of unusual interest since inheritance is Mendelian dominant in type, most of the progeny being affected. Of even more significance is the fact that the mating of two individuals with the mild disease may result in severe Cooley's anemia in one or more of the children.

Since target cells and increased hypotonic resistance are common in sickle-cell anemia, and since there are many other features of resemblance with the target-cell syndromes, the possibility was

*This exhibit has been reprinted in book form (*Hemolytic Syndromes.* By William Dameshek, M.D., Tibor J. Greenwalt, M.D., Russell J. Tat, M.D., and Camille Dreyfus, M.D. 43 pp. Boston: The Bailey Press, 1942.)

advanced that the Mediterranean target-cell disease might be related to the essentially African target-sickle-cell syndromes. Transitional forms between the two syndromes have been found. Heart murmurs, usually rough systolic in type, are noted in both conditions. In a young Negro child it is often difficult to determine whether the murmur is of rheumatic origin or due to the sickle-cell anemia. Spells of fever and joint pains are common in both conditions, and it is therefore necessary in every case to rule out sickle-cell anemia and the sickling trait. These points are discussed by Walker and Murphy[61] and by Klinefelter.[62] The former authors report an unusual case in which sickle-cell anemia was complicated by acute rheumatic heart disease. Klinefelter attributes all the cardiac findings in sickle-cell anemia to diffuse enlargement of the heart with resultant systolic and diastolic murmurs and prolongation of the PR interval in the electrocardiogram. Although he believes that the cardiac changes are secondary to the severe long-standing anemia, this often seems unlikely since the murmurs are often very striking and the anemia very mild. What is more, cases of severe hypochromic, hemolytic and pernicious anemia usually fail to show murmurs of such degree of severity.

Familial hemolytic jaundice should be differentiated from a familial nonhemolytic variety that was recently described by Dameshek and Singer.[63] Although the jaundice is familial, hereditary and acholuric, and associated with the presence of indirect bilirubin in the blood, there are no evidences of increased blood destruction. There is no splenomegaly, and the blood-cell and reticulocyte counts are normal. The bile-pigment output as measured by the fecal urobilinogen is low. Why, then, the jaundice? This appears to be due to a constitutional hepatic dysfunction, the liver cells being unable to remove bilirubin from the blood stream at a normal rate. Thus there seems to be a specific physiologic dysfunction in bilirubin excretion, since other liver-function tests are completely negative and biopsy of the liver is normal.[64] The incidence of this disorder is much higher than has been suspected. Many cases of mild jaundice probably fall into this category.[65] The importance of the condition lies in the fact that it is commonly mistaken either for familial hemolytic jaundice or for hepatic disease. Other than diagnostically, it appears to have no great significance, since a number of persons in these families have been known to reach old age.

Acquired Types

The results of splenectomy in the hemolytic crisis of familial spherocytosis are as a rule excellent, but there is still disagreement regarding its value in the acute cases of the acquired groups. Thus, Sharpe and Tollman[66] in describing 5 cases of "refractory hemolytic anemia" found that transfusions produced dangerous and alarming reactions in 2 cases and that splenectomy in each case failed to modify the course of the disease. The latter statement is not borne out by the case reports. Thus, in Case 1 the patient slowly recovered after operation, whereas prior to it the course had been progressively downhill. Case 2 was obviously not one of hemolytic anemia (no anemia, normal reticulocyte count, direct bilirubinemia and so forth). In Case 3, in which the patient was desperately ill, there was prompt improvement in the blood and progressive decrease of the jaundice with slow but complete recovery. In Case 4, the diagnosis of hemolytic anemia must be considered as extremely doubtful, since there was no record of bilirubin estimation, the reticulocyte percentage was only 2.4 per cent, and the leukocyte and polymorphonuclear counts were very low. In Case 5, splenectomy was postponed until the hemoglobin percentage was 16, and the red-cell count 510,000! It was then performed as an emergency measure and the patient died shortly afterward. Thus of the five so-called "refractory cases" reported, 2 may not have been hemolytic anemia, in 2 the patient recovered, and in 1 procrastination may have been at least partly responsible for the poor result.

Jackson, Parker and Lemon[67] claim that some cases of "agnogenic" (idiopathic) myeloid metaplasia of the spleen masquerade as hemolytic anemia and that it is important not to remove the spleen because blood cells are being produced there. However, in hemolytic anemia it can be shown that the bone marrow is extremely hyperplastic in response to hemolysis and that myeloid metaplasia of the spleen and liver is a frequent occurrence. Brewster and Wollenman,[68] apparently accepting Jackson's viewpoint, have recently reported a case of acute acquired hemolytic anemia with spherocytosis in which splenectomy was unsuccessful. The myeloid metaplasia is stressed and the intimation is made that this case probably belongs in Jackson's group. I have seen marked myeloid metaplasia both of the spleen and liver in patients who have *recovered* after splenectomy, and this is not surprising in view of widespread regenerative activity in response to hemolysis.

My own conception of the value of splenectomy in acquired hemolytic anemia is based on a study of 18 splenectomized cases, of which 10 made full recoveries and 8 died.[69] Although this mortality rate is undoubtedly high, it included a number of procrastinated and desperate cases. In these cases, the high mortality with splenectomy (about 40

per cent) must be balanced against the almost certain 100 per cent mortality involved in the policy of "waiting for something to turn up." It is quite impossible in a given case to state categorically whether or not recovery will take place; however, it is unwarranted to withhold operation, which may prove dramatically successful. Temporization, which involves many transfusions, may result in irreversible hemolysis for which splenectomy is often valueless. If the patient fails to respond to two or three transfusions, splenectomy should be done.

One of the acquired hemolytic anemias in which splenectomy has no effect is that curious condition known as paroxysmal nocturnal hemoglobinuria. In this disease, there are chronic hemolytic anemia, persistent hemosiderinuria and paroxysms of nocturnal hemoglobinuria. The mechanisms are completely obscure. The red cells of this disease are unusually susceptible to hemolysis by dilute acid, and the acid fragility test therefore becomes of great importance in the diagnosis of an acquired case in which hemoglobinuria may not be prominent. Both why the red cells are broken down intravascularly (only in the kidneys?) and why hemosiderinuria is always present are mysteries. Experiments that may have a bearing on some of these points are presented by Yuile, Steinman, Hahn and Clark.[70] These authors noted a drop in the renal threshold for hemoglobin in dogs after repeated injections, together with dense deposits of iron-staining pigment in the convoluted tubules — findings that are present in the above disease. These and other data are summarized in a review article on hemoglobinuria by Yuile.[71]

Methods

By the use of the Evelyn photoelectric colorimeter, it is possible to differentiate readily and quantitatively between the prompt (direct) bilirubin and the delayed (indirect) type. Lepehne[72] and Cantarow, Wirts and Hollander[73] have investigated these phenomena. Cantarow et al., recommend the quantitation in each case studied of both indirect and direct bilirubin, since if the direct bilirubin is increased either absolutely or relatively, it indicates some degree of hepatic impairment. The use of the bile-pigment output, chiefly the fecal urobilinogen, and of the hemolytic index in the measurement of hemolysis is stressed by Miller, Singer and Dameshek.[74] These observers state that of the various indexes of possibly increased hemolysis — acholuric jaundice, indirect bilirubinemia, an increase in the urinary excretion of urobilinogen, anemia and leukocytosis — no one is specific. An increase in the daily fecal output of urobilinogen or in the hemolytic index is, however, unequivocal evidence of an increased breakdown of blood. The latter index relates the output of bile pigment to the total grams of circulating hemoglobin from which the urobilinogen is derived. Thus the output of 200 mg. of daily fecal urobilinogen at a level of 5 gm. of hemoglobin per 100 cc. of blood represents three times as much destruction as the same output at a 15-gm. level. This holds true for children as well. A male adult weighing about one hundred and fifty pounds excretes over 150 mg. of urobilinogen. This amount in a fifty-pound child represents about three-times-normal value. The urobilinogen output following transfusions of stored and fresh blood was studied by Wasserman, Volterra and Rosenthal.[75] The excretion of bile pigment after transfusion with stored blood was far higher than after transfusion with fresh blood, being directly proportional to the length of time of blood storage. Blood stored for more than seven days was so readily broken down that the authors concluded that its use was inadvisable in anemia. According to my own experience, the use of stored or bank blood, however fresh, should be reserved for hemorrhage or shock. For any of the so-called "blood dyscrasias" — whether concerned with the red cells, white cells or platelets — fresh citrated blood is best.

The osmometric behavior of normal human erythrocytes has been studied by Guest and Wing[76] by the use of an ingenious method in which the degree of actual swelling of the red cells under conditions of hypotonicity could be studied. These experiments indicated that normal human erythrocytes are perfect osmometers, that is, they behave mathematically correctly with reference to swelling in relation to the various hypotonic salt solutions. By means of a radioactive iron technic for tagging the red cells, Cruz, Hahn, Bale and Balfour[77] reached the surprising conclusion that old cells are far more resistant to hypotonic salt solutions than new cells (reticulocytes). This is contrary to what one might expect physiologically.

Hemorrhagic Diatheses

Lozner[78] states: "The body, when injured, possesses two main defenses against the occurrence of hemorrhage. . . . These may be called the blood coagulability defense and vascular defense." The blood-coagulability defense may in general be subdivided into two headings, comprising the platelets and the various chemical or enzymatic factors that are concerned in making blood clot when it is shed. Thus three main types of hemorrhagic diathesis may be discriminated: that which is associated with a disturbance in one or more of the chemical factors, such as calcium, thromboplastin, prothrombin, thrombin, fibrinogen, fibrin and antithrombin; that due to a deficiency or defect

of the blood platelets; and that secondary to a disturbance in the capillary walls. The first two may properly be grouped in the blood dyscrasias; the third is a vascular condition.

Methods

Ivy, Nelson and Bucher[79] describe a standardized cutaneous venostasis bleeding-time technic in which the skin of the forearm is used, venostasis being produced by a pressure of 40 mm. of mercury from a sphygmomanometer cuff. The normal mean bleeding time by this method was 61.56 (± 2.08) seconds. To control most of the known factors that influence the bleeding time, Copley and Lalich[80] devised a so-called "hemorrhagemeter," in which the principle of bleeding into fluid kept constantly at 37°C. was used. In addition to the red-cell or blood flow, a whitish flow was observed, which was believed to be mostly lymph, and thus a "lymph time" was suggested. The normal bleeding time by this method was 170 to 180 seconds, which is quite comparable to the Duke bleeding time, in which a simple puncture of the ear is performed. Lozner, Taylor and MacDonald[81] studied the effect of foreign surfaces on blood coagulation. Glass apparently has a definite effect in causing blood to clot rapidly, since the same blood in paraffin-treated or plastic (Lusteroid) tubes shows a far longer clotting time: that is, glass eleven minutes, paraffin forty-four minutes and plastic forty-nine minutes. This difference is probably due to the presence of negatively charged ions on the glass surface. It is fortunate that the capillary endothelial surfaces behave more like plastic than like glass. At any rate, the surface with which the blood comes in contact must also be considered in the blood-clotting problem.

Although Quick's method for determining prothrombin in the blood is almost universally accepted, modifications are constantly being published. It is true, as Quick himself stated, that his and other tests are based on an unproved assumption — namely, that they actually measure prothrombin — and "therefore the validity of the results which they yield can be judged only by correlation with clinical observation." Copley[82] believes that the term "prothrombin concentration" may be inaccurate and says that the term "prothrombin time" is to be preferred. Cheney[83] presents a simplified plasma-coagulation time in which recalcification is carried out but thromboplastin (rabbit brain) is not used. He contends that the addition of thromboplastin is unnecessary and that the test is satisfactory for vitamin K deficiency provided the physical conditions of the procedure are closely adhered to. A "one-minute bedside prothrombin method" is described by Rhorer,[84] who states that it gives results quite comparable to other more difficult and time-consuming tests. A large drop of blood is allowed to fall into the hollow of a suitable glass slide, following which thromboplastin is added and the coagulation time observed.

The failure of circulating blood to clot spontaneously in vivo still remains an obscure phenomenon, according to Wilson,[85] since all the elements essential for immediate coagulation in vitro are apparently present. Howell has consistently maintained that there is an antithrombic substance in the blood. This might be heparin. His views are summarized in his recent article.[86] Wilson describes a method for the determination of antithrombin in blood serum and plasma and finds that normal blood contains an average of 90 units of this substance per cubic centimeter. He states that the hemorrhagic tendency in hypoprothombinemia is not fully explained on the basis of decreased prothrombin but that hemorrhage usually occurs when the prothrombin unitage approximates or is lower than the antithrombin unitage. Tagnon[87] describes a method for obtaining from oxalated plasma a proteolytic enzyme active in blood coagulation. This enzyme appears to play a primary role in the mechanism of blood coagulation and its absence may be the cause of hemophilia.

Bell, Lazarus and Munro[88] describe a standardized method for the determination of capillary fragility based on Gothlin's method of 1931 and similar to that worked out more recently in this country by Wright and Lilienfeld.[89] A circle is measured over the forearm and a blood-pressure cuff is inflated over the upper arm for fifteen minutes at 50 mm. The petechiae are counted with the naked eye. A petechial count below eight can be regarded as normal, whereas eight or more petechiae require further investigation. In women near the menstrual cycle and in individuals with diminished ascorbic acid levels, the petechial count may be increased. If these factors can be excluded, a high petechial count is definitely abnormal.

Clinical Features

Hypoprothrombinemia. Sanford and Shmigelsky[90] studied in infants the question whether the presence of bile and food in the small intestine is necessary for the formation of prothrombin. They concluded that the present explanation of the synthesis of vitamin K by bacteria in the small intestine and the necessity of bile for its conversion is untenable. The liver appears to be the principal source of this vitamin and continues to form it independently of extrinsic causes until its functions are diminished by serious damage. The chemistry of vitamin K is fully (and readably) discussed by Fieser,[91] one of the leaders in this field. A

rarity, namely a case of idiopathic hypoprothrombinemia in a boy of eighteen, is described by Rhoads and Fitz-Hugh.[92] The case had previously been classified as an atypical one of hemophilia because of a persistent tendency to bleed. In another article on experimental hypoprothrombinemia, Rhoads, Warren and Panzer[93] state that a reduction of plasma prothrombin has been effected experimentally by at least ten different means, including modifications of the diet, the liver and the bile ducts, as well as through sweet-clover disease. Clinically, hypoprothrombinemia may be due to dietary K avitaminosis; to a conditional K avitaminosis secondary to the absence of bile salts from the intestinal tract and to liver injury of sufficient degree to prevent synthesis of prothrombin at an adequate rate. The latter condition does not respond to vitamin K therapy, the first one responds quickly, and conditioned vitamin K deficiency requires bile salts in addition to oral vitamin K.

The administration of vitamin K to women in or just before childbirth has been recommended as a routine procedure. It is well to remember that many newborn infants have a low concentration of prothrombin without presenting any evidence of hemorrhagic disease. If the concentration of prothrombin in the blood can be raised prior to the rigorous journey through the birth canal, it is probable that intracranial hemorrhage and its distressing sequelae can be largely avoided. Mull, Bill and Skowronska[94] recommend 1 mg. of the vitamin orally, four to ten hours before delivery. Most authors recommend the intramuscular injection of a vitamin K preparation during the first stage of labor, especially since gastrointestinal absorption by the mother may be subject to much fluctuation. Infants of mothers treated with vitamin K usually present a normal prothrombin time, quite in contrast to those from untreated mothers. Infants with clinical evidence of hypoprothrombinemia can be treated with 1 mg. orally at eight-hour intervals for a day.

Knowledge that the hemorrhagic sweet-clover disease of cattle is due to hypoprothrombinemia has led to a series of brilliant investigations, chiefly by Link and his associates of the University of Wisconsin, culminating in the synthesis of 3,3′-methylenebis (4-hydroxycoumarin). This substance, when given orally, produces a well-marked reduction in prothrombin and can thus be used to diminish the coagulability of the blood. Bingham, Meyer and Pohle[95] and Meyer, Bingham and Axelrod[96] report on the experimental and clinical aspects of dicoumarin administration. The substance is given orally in an initial dose of 5 mg. per kilogram of body weight, with daily doses thereafter of 1.5 mg. per kilogram. Since individual responses vary considerably, it is necessary to control the prothrombin and coagulation times frequently. Cautiously used, dicoumarin may be of value in conditions with impending or active thrombosis or following splenectomy. Because of the ever-present possibility of hemorrhage (cerebral, renal and so forth) its present use should be limited to patients kept under carefully controlled observation. Administration of vitamin K will not correct the prothrombin deficiency induced by the drug.

The thrombic activity of a globulin fraction derived from rabbit plasma and the use of rabbit thrombin as a local hemostatic were described by Lozner, Taylor and Taylor[97] and were mentioned in last year's review. For local use, a square of saline-moistened filter paper is placed over the dry powdered rabbit thrombin (Lederle) that has been applied to the wound. This therapeutic procedure should prove of great value in the control of local bleeding and has even been found effective as a local application to bleeding surfaces. The treatment of the latter disease still remains unsatisfactory, however, chief reliance being placed on transfusions of blood. Johnson[98] points out that certain difficulties are involved in transfusions, namely the necessity of typing and cross-matching and the possibility of building up intragroup incompatibilities with repeated transfusions. Johnson used dry plasma from blood that had been processed within the first few hours after removal from the donor. Keeping blood for seven days before lyophilization resulted in a very definite reduction in its thromboplastic activity. However, dry plasma that had been kept for months at 5°C. showed no reduction in its clot-promoting property. The average dose of plasma used was 125 to 150 cc.; typing of the plasma was found unnecessary, even with unpooled plasma. Prophylactically, one of the most satisfying results of the use of lyophile plasma was the elimination of the fear of dental extractions. Thus, a dose of 150 cc. of plasma given prior to extractions reduced the coagulation time to normal; following extractions, the sockets were packed with dry plasma. Almost complete rehabilitation of one patient with severe hemophilia was accomplished by the use of injections of 125 cc. plasma given weekly for three months.

A fascinating series of studies on a hereditary hemophilia-like disease in swine is reported by Muhrer, Hogan and Bogart.[99]

The Spleen

The spleen still remains an organ "full of mystery." Hints of its various functions may be obtained, however, by removing it or by studying it

in relation to various clinical conditions. Studies of splenectomized material by Singer, Miller and Dameshek[100] disclosed an intimate spleen-marrow relation, a definite influence of the spleen on the thickness of the red cells and a similar influence on blood destruction. Following splenectomy, the leukocyte and platelet counts almost always increase, indicating (with bone-marrow studies) that the spleen normally exerts an inhibitory effect on the bone-marrow production of these cells. Howell-Jolly bodies and nucleated red cells, especially in abnormal states, appear in the peripheral blood, suggesting an influence of that organ on denucleation of the red cells. The red-cell population becomes thinner, as evidenced not only by various measurements but by an increased hypotonic resistance and the presence of target cells. The red cells, in their various passages through the spleen, probably become thicker and thicker and thus more hypotonically fragile; with the spleen removed, this process is retarded and the target cell becomes evident. This was shown experimentally by Miller, Singer and Dameshek[101] in dogs and guinea pigs. Cruz and Robscheit-Robbins[102] found that in splenectomized dogs made anemic by bleeding or by the injection of acetylphenylhydrazine, the number of normoblasts in the peripheral blood during the first phase of the regenerative period was four times greater than that in the nonsplenectomized animal. These findings were also suggestive of a spleen-marrow relation, the spleen appearing to have an effect on the maturation or delivery of the nucleated red cell. I[103] have discussed various facts and fancies relating to the spleen, including such concepts as "hypersplenism." Normal hypersplenism, which occurs when the spleen is enlarged for almost any cause — infection, congestion, cirrhosis of the liver or splenic vein thrombosis — usually results in leukopenia, thrombocytopenia and granulocytopenia, and often in anemia. Despite the low counts in peripheral blood, the bone marrow is hyperplastic; immediately following splenectomy, the leukocyte and platelet counts rise and remain elevated. These findings may indicate a hypernormal effect of the spleen on the marrow. Abnormal hypersplenism is present when for some unknown reason the spleen exerts an unusual effect on the marrow, with resultant hemolytic anemia or thrombocytopenic purpura. In the latter condition, despite the lack of platelets in the peripheral blood, the marrow is crowded with megakaryocytes, which, however, fail to produce platelets. Directly after splenectomy, the megakaryocytes show intense platelet production and the platelet count increases rapidly. If these interpretations of the relations of the spleen and the marrow are correct, they indicate the elaboration by the spleen of hormones that have effects on the centers of red-cell, white-cell and platelet production in the marrow. The evidence is as yet purely circumstantial and must await further investigation for complete proof.

Felty's syndrome has recently received increasing attention. This is a disorder in which marked rheumatoid arthritis, splenomegaly and leukopenia are simultaneously present. Lockie, Sanes and Vaughan[104] adhere to Felty's original concept that, owing to the chronic rheumatoid infection, the spleen becomes affected and the leukocyte count is lowered. The sternal marrow in their 2 cases showed slight myeloid hyperplasia, and the spleen chronic nonspecific splenitis. Steinberg[105] points out that the leukopenia and the secondary anemia characteristic of the syndrome are not due to bone-marrow depression, since sternal-marrow biopsies showed a hyperplastic marrow. As he states, it seemed plausible that the spleen may act as a barrier in not permitting the blood to receive these cells in sufficient quantities. Splenectomy was accordingly performed in 1 case with a marked and permanent effect in bringing the leukocyte count to normal. In a similar case seen by me, the patient's leukopenia and neutropenia were so marked that she was subject to numerous attacks of pyogenic infection. The leukocyte count averaged 1000, with approximately 10 per cent polymorphonuclear leukocytes. Splenectomy was performed with the idea of bringing the leukocyte count to normal, especially since the bone marrow was found to show extreme hyperplasia of the leukopoietic tissue. Following operation, the white-cell count returned to normal and further infections did not occur. The platelet count, which also had been somewhat depressed, rose to normal levels and the patient's menorrhagia was alleviated. The results in these cases are probably related to the very interesting concept of primary splenic neutropenia developed by Wiseman and Doan.[106] The essential condition in 5 cases was profound granulopenia, panhyperplasia of the marrow and splenomegaly and recovery after splenectomy. Varying degrees of combination of hemolytic anemia and thrombocytopenia purpura were encountered and also corrected by splenectomy. It was assumed that a single mechanism — hypersplenism — was responsible for the anemia, leukopenia and thrombopenia, since all elements were increased after splenectomy. Thus, one may group primary splenic neutropenia with hemolytic anemia and thrombocytopenic purpura; all of which may be due to abnormal hypersplenism, as stated above.

Until recently, most cases presenting splenomegaly were immediately called Banti's disease or splenic anemia. Whether any such condition as

postulated by Banti exists is greatly to be questioned. Cirrhosis of the liver, splenic-vein thrombosis or portal hypertension due to various causes may result in splenomegaly, anemia and leukopenia. Similarly, Gaucher's disease, Boeck's sarcoid of the spleen and Felty's syndrome, as noted above, may all result in anemia, leukopenia and thrombopenia that respond to splenectomy. Banti's disease and splenic anemia are best considered as "wastebasket" diagnoses reserved for those cases that have either been studied superficially or in which all other diseases have been excluded. In the last year or two, "agnogenic myeloid metaplasia," as introduced by Jackson, Parker, and Lemon,[67] has vied with Banti's disease as the diagnosis in many cases of splenomegaly. The contention inherent in this rather impressive-sounding term is that the spleen may be the site, for no known cause (agnogenically), of active but ectopic bone-marrow hyperplasia. That the spleen ever develops myeloid metaplasia independently, except in chronic myelogenous leukemia, is to be seriously questioned. Fibrosis, sclerosis or aplasia of the bone marrow, or its invasion by leukemia, lymphosarcoma, Gaucher's disease and so forth, may result in such extensive depletion of the normal bone marrow that various tissues attempt to take up the burden. This is customarily done by embryonically active hematopoietic organs such as the spleen and the liver, but such organs as the lungs and the adrenal glands may participate.

The end-result of bone-marrow displacement plus myeloid metaplasia in the spleen is often a blood picture characterized by normocytic anemia, leukocytosis with the presence of immature granulocytes, reticulocytosis and polychromatophilia, together with the presence of nucleated red cells. The blood picture (and the splenomegaly) may thus resemble chronic myelogenous leukemia, but the trephine bone-marrow biopsy shows the true marrow condition, which is either that of fibrosis or of replacement by various abnormal cells. Polycythemia vera may terminate in a similar end-picture frequently miscalled chronic myelogenous leukemia. Severe hemolytic anemia of the acquired type, particularly if it is of several months' duration, may also result in myeloid metaplasia of the spleen and liver. Jackson and his collaborators contend, however, that the metaplasia of the spleen may be inherent in that organ and that hemolytic jaundice, osteosclerosis, fibrosis of marrow and so forth, are simply accompanying rather than primary features. If this is the case, it would be indeed harmful, as these authors maintain, to remove the spleen or treat it by x-ray, since this organ is producing useful blood cells. Setting aside the matter of whether the splenic disorder is primary or not, it seems to me that a carefully done sternal trephine bone-marrow biopsy should help to settle this question. If the marrow is aplastic, fibrotic or invaded by foreign tissue, splenectomy should certainly not be performed; if, on the other hand, it is hyperplastic and the patient shows hemolytic anemia, removal of the spleen should be seriously considered. Reich and Rumsey[107] recommend biopsy of the spleen through the peritoneoscope in doubtful cases. They state that the presence of myeloid metaplasia definitely establishes the diagnosis of agnogenic myeloid metaplasia of the spleen. This is quite contrary to my views, as stated above, and also to some of Reich and Rumsey's own case reports. Thus in Case 2 when a bone-marrow biopsy was finally done — after splenectomy — it showed fibrosis. In Case 3, there was slight jaundice and the red-cell count rose from 3,000,000 to 6,000,000 after splenectomy; this case might well have been one of hemolytic anemia. In Case 4, which showed myelocytes in the blood and an essentially normal marrow at puncture biopsy, the white-cell count after splenectomy rose to 134,000 (!), which might well indicate that leukemia was present. Case 5, which presented a fairly typical picture of hemolytic anemia, was not splenectomized. At autopsy, the bone marrow was erythroblastic. Critical examination of these cases leads one to suspect that enthusiasm for a "new" syndrome may result first in calling many diverse types of cases examples of this condition, and secondly in withholding appropriate therapy, like splenectomy, from certain others. That fibrosis of the marrow, particularly after polycythemia, occurs and is associated with a leukemoid blood picture and myeloid metaplasia of the spleen is quite certain. That the latter is ever primary is, however, questionable.

Primary neoplasms of the spleen are rare. I have recently seen a case of primary lymphosarcoma and one apparently of primary Hodgkin's disease of that organ. Pines and Rabinovitch[108] give a full report of a case of hemangioma of the spleen. An interesting neoplasm is that of hamartoma, as described by Sweet and Warren.[109] Here the spleen is the site of a neoplasm or neoplasms composed of new but normal splenic tissue.

The days when splenectomy was performed for almost any enlargement of the spleen have practically gone. Splenomegaly may be due to a large number of diverse conditions. In general, these are: infections (typhoid fever, malaria, syphilis, tuberculosis, Boeck's sarcoid and so forth); hyperplasias (leukemia, Hodgkin's disease, lymphomas and myeloid metaplasia); increased blood destruction (hemolytic anemias of various types); portal hypertension (cirrhosis of the liver and so forth); storage disorders (Gaucher's disease and so forth); and increased blood volume (polycythemia). Determination of the cause of the enlarged spleen in a

given case may be quite difficult, requiring careful and at times intricate studies of the blood, bone marrow and bones, the liver function, the serology, the esophagus (for varices) and so on. Puncture biopsy of the spleen, which is recommended by some workers as a harmless procedure and of considerable diagnostic value, should not be undertaken too lightly because of the danger of hemorrhage.

Splenectomy must be considered primarily from the physiologic standpoint and not from that of the degree of splenic enlargement. Some of the largest spleens are seen in cases of chronic myelogenous leukemia and polycythemia and in occasional cases of Hodgkin's disease; these are best left alone. Some of the smallest spleens may cause the greatest trouble, as in thrombocytopenic purpura and leukopenia.

Definite indications for splenectomy are severe fulminating thrombocytopenic purpura and severe acute or subacute hemolytic anemia. In both these conditions, it is presupposed that definite causes for the purpura and the hemolytic reaction have been ruled out. To procrastinate in either condition is to invite disaster, either from hemorrhage in the first instance, or from persistent hemolysis in the second. In mild cases of idiopathic thrombopenic purpura, splenectomy need not be seriously considered. There is a growing indication for splenectomy in severe leukopenia and granulocytopenia, provided various well-defined causes, such as leukemia (aleukemic), aplasia and Hodgkin's disease, can be ruled out by bone-marrow studies. As noted above, Felty's syndrome with marked leukopenia may be a perfectly good indication. This may also hold true in Boeck's sarcoid, Gaucher's disease and portal hypertension when one or several of the triad of thrombocytopenia, leukopenia and increased hemolysis are present to a marked degree. Whether the spleen should be removed routinely in cases of portal hypertension, particularly when the liver is thought to be normal (splenic-vein thrombosis and Banti's disease), is debatable. In an excellent article on the present status of surgery of the spleen, Pemberton[110] states that splenectomy in Banti's syndrome "lightens the load that has been thrown on the liver by reducing the volume of blood entering the portal circulation, removes possible toxic substances originating in the spleen, removes the splenic factor in blood destruction and produces adhesions for the establishment of collateral circulation." Although I cannot be quite so optimistic, it must be admitted that there is probably some justification for these statements. The end-results of a five-year or ten-year study in a sufficient number of cases of portal hypertension, splenectomized and nonsplenectomized, with and without hematemesis, are not yet at hand. Pending this, the ultimate value of splenectomy in this group of cases must be kept *sub judice*. Occasionally, the spleen should come out because its large bulk in a child actually interferes with locomotion and therefore with further physical development. I have had this done in cases of Gaucher's disease, Cooley's anemia and sickle-cell anemia, with results that have been, at least temporarily, excellent.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 29061

PRESENTATION OF CASE

A forty-eight-year-old Polish garment worker entered the hospital because of abdominal pain and weight loss.

Four months before entry the patient developed a rather vague upper abdominal pain, which was most marked on pressure over a point midway between the xiphoid and umbilicus. The pain was usually relieved by drinking milk and aggravated after eating meat. The patient occasionally felt nauseated but seldom vomited. Laxatives at first relieved the pain, but after a few weeks even these proved ineffective. He also noted swelling of the abdomen and ankles, the latter being present in the morning as well as the evening. Three months before entry he was seen in the Out Patient Department, where physical examination revealed a somewhat distended but nontender abdomen. The liver edge was palpable on deep inspiration, and the upper level of liver dullness was percussed to the fourth interspace. The spleen was not felt. Normal peristaltic sounds were audible. There was questionable bilateral ankle edema. Examination of the blood was not remarkable, and both a barium meal and a barium enema were negative. A chest roentgenogram showed a high diaphragm on both sides, with linear areas of atelectasis in the lungs. The heart was transverse in position and not enlarged. The aorta was remarkably tortuous but showed no actual widening. During the next three months, despite extensive study, no diagnosis was established. On one examination shifting dullness in the abdomen was found. A bromsulfalein test showed 5 per cent retention of the dye in the serum. During the period of illness he lost 20 pounds. He denied diarrhea, tarry, bloody or acholic stools, dysuria, pyuria and hematuria. He had suffered with nocturia (two times) for several years. Because of the persistence of symptoms and the lack of a diagnosis, hospital admission was advised.

The family history was noncontributory. The past history was not remarkable, except that the patient had always consumed large amounts of wine and beer.

Physical examination on admission revealed a well-developed man who did not appear to be in great distress. He had obviously lost a great deal of weight. The edges of the tongue were smooth and somewhat redder than normal. Examination of the heart and lungs was normal. The abdomen was full, particularly in the right lower quadrant, where no mass could be felt but percussion demonstrated a localized area of flatness. In the upper abdomen, the rectus muscles were separated in the midline for a distance of 4 cm. There was tenderness in the left calf on palpation and on movement of the left ankle. The left leg was 32 cm. in circumference at the calf and the right 31 cm. The left foot seemed warmer than the right, and the pulsation of the dorsalis pedis artery was stronger on the right than on the left.

The blood pressure was 165 systolic, 102 diastolic. The temperature was 98.6°F., the pulse 92, and the respirations 15. The temperature ranged between 97 and 101°F. and the pulse between 70 and 120 on the four succeeding days.

Examination of the blood revealed a hemoglobin of 74 per cent, a red-cell count of 4,500,000 and a white-cell count of 10,300, with 64 per cent polymorphonuclear leukocytes. The urine was normal. The stool was guaiac negative on three examinations. The blood Hinton test was negative, and another gastrointestinal x-ray series was negative.

A peritoneoscopy was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. CHESTER M. JONES: "Four months before entry the patient developed a rather vague upper abdominal pain, which was most marked on pressure over a point midway between the xiphoid and umbilicus." I suppose they mean tenderness that was increased by pressure rather than pain that the patient felt.

The physical examination apparently confirms the patient's statement that there was pain on pressure in the midabdomen. The examination also seems to indicate that the liver really was enlarged.

The high diaphragm by x-ray might have been due to the large liver or to abdominal distention. The linear areas of atelectasis probably meant old pulmonary infarcts.

"The patient had always consumed large amounts of wine and beer." I suppose that is an attempt to sell me a diagnosis.

According to the record it seems clear that it was at first believed that this patient had cirrhosis of the liver. But as the story develops there are many discrepancies so far as such a diagnosis is concerned. I am sure that I am not going to be

able to give a diagnosis that will be any more than tentative, but there are certain facts I should like to point out.

There is no mention of rectal examination but something was felt in the right lower quadrant. Was a rectal examination done on this patient?

DR. TRACY B. MALLORY: Yes. The right lobe of the prostate felt harder than normal but seemed to be normal in size.

DR. JONES: Would you trust a statement of that sort, Dr. Colby?

DR. FLETCHER H. COLBY: Not entirely.

DR. JONES: Neither should I. One should state that rectal examination showed an asymmetrical prostate, the right lobe being harder than normal. Another point should be made — namely, that no rectal mass was felt outside the prostate; that is important.

So far as the x-ray films are concerned, the heart is transverse, and I shall pay no attention to it. There seems to be a suggestion of displacement of the small bowel from the right lower abdominal quadrant. Certainly the x-ray findings are not distinct nor do they appear to be helpful. One thing can be said: there is no evidence of intrinsic gastrointestinal disease. It is also important, if we have the right to make the statement, that no esophageal varices were demonstrated. I assume that, with two gastrointestinal series, varices were looked for and apparently not demonstrated. This is an oblique film, and I should not say that the stomach or duodenum is displaced, nor is the duodenal curve. At least there is lack of evidence of an extrinsic pressure defect around the stomach or duodenum. This is a good picture of the jejunum without any evidence of disease.

The story is short — apparently four months — and is entirely consistent with a new growth, either primary or secondary to what had hitherto been a silent cirrhosis. He had a tremendous loss of weight, — 20 pounds in four months, — without much vomiting. To be sure it was probably due to a lack of food intake, but it occurred. The patient had a mass with vague gastrointestinal symptoms. There is nothing in the record that gives any clue concerning the nature of the pain. It is poorly described. One can say that neoplasm should be seriously considered. We are hard pressed to believe that it was ulcer pain. It was not relieved by the things that relieve ulcer — milk, soda and so forth. The statement that meat made the pain worse is curious.

DR. MALLORY: He evidently gave a confusing story, Dr. Jones. The record says, "A very confusing story but the point which on reiteration seems definite is that the present illness came on within the past year and consisted of a constant aching pain just above the umbilicus that was worse after eating a heavy meal and not definitely relieved by milk."

DR. JONES: One can say that it is an atypical story. There is nothing characteristic about it, and this fact is against the diagnosis of peptic ulcer. There are no cardiorespiratory symptoms, a point worth something in excluding certain diagnoses. Another fact that should be pointed out is that for two years he had had nocturia, never having previously noted it. I gather there was more or less language difficulty and that it was impossible to get an accurate story.

On physical examination the patient was emaciated and showed definite evidence of deficiency disease, which was probably secondary rather than the cause of the symptoms. It was evidenced by a loss of weight, a smooth red tongue, and, possibly, the appearance of edema from time to time. The liver on examination was palpable on inspiration, and the upper edge was at the fourth interspace or fifth rib. The diaphragm was certainly high, and it is quite possible that this patient really had a big liver, but at the time of physical examination on admission to the hospital absolutely nothing is said about the liver so one has the right to be skeptical about the enlargement noted in the Out Patient Department. I am not at all sure the liver was enlarged. If it was, then it subsequently diminished in size. The spleen was not palpable at any time. There is a definite note made to that effect. From these films, so far as I can tell, it seems fair to say that the spleen is not enlarged. If this patient had cirrhosis of the liver, which I doubt, with the edema and ascites that are supposed to have been noted one should expect to have been able to demonstrate some enlargement of the spleen.

On admission there were other physical findings that may be of importance — namely, signs of thrombophlebitis in the left leg, with an area of tenderness, increased warmth and possibly some edema. There was evidence of tortuosity of the aorta and of arteriosclerosis. But I think these two factors do not need to interest us too much. There was no anemia of importance. At least on one examination the lungs and heart were normal. The urine and stools were normal, and a Hinton test was negative. The bromsulfalein test showed 5 per cent retention at the end of half an hour. In other words, the laboratory findings are not diagnostic or helpful. All the x-ray studies were reported to be negative and serve only to exclude disease rather than to make a diagnosis. Fever was present, without leukocytosis. If this patient had a thrombophlebitis it is possible that the elevation of temperature to 101°F. may have been

due to a local inflammatory process in the leg. It is curious that there was no leukocytosis. I am inclined to think that the fever was due in part to what was going on in the leg. If there was intrahepatic disease, that fact, regardless of the nature of the disease, would lead us to expect slight elevation in temperature from time to time.

With these facts, or near facts, and negative findings, how can one make a diagnosis? I do not believe it is possible. The important thing to do is to arrive at the decision of what to do, having excluded certain things. Cancer of the gastrointestinal tract seems unlikely. It is possible to have a small lesion of the colon, miss it on the x-ray films and have the liver full of metastases. We have seen such cases. However, there is no evidence that this is the case here. The stool was negative, and there was no evidence of occult bleeding. Everything is against gastrointestinal cancer. Again, so far as one can tell there is no evidence of pancreatic enlargement. A cancer of the pancreas, clinically, is unlikely, and I think it was not present.

Did this patient have cirrhosis of the liver? He had an alcoholic history and a palpable liver on one occasion, he was said to have had shifting dullness in the abdomen, and he had edema on a few occasions in the legs. If that story is true one must entertain the diagnosis of cirrhosis of the liver. One fact in favor of it is the indefinite gastrointestinal story, but against it are the demonstration of an enlarged liver at the second examination, the failure to demonstrate the spleen or esophageal varices and the absence of retention of dye. If edema and ascites are associated with cirrhosis, one would expect to get a more specific set of findings than are available here. Furthermore, there was no anemia, and usually the patient with cirrhosis that comes into the hospital is moderately anemic. Therefore, I think that the logical diagnosis is not that of cirrhosis. We have seen many cirrhotic patients in this hospital whose symptoms are not due to the lesions of the liver; such a cirrhosis in a sense may be called compensated and not the dominant part of the history. The cirrhosis here, if it was cirrhosis, was not the cause of the symptoms. If that is true, how can we explain them on the basis of the findings we have? I confess I cannot do it. The best I can do is to suggest that he had a malignant tumor that had not been located. There is one curious statement — namely, that there was no mass in the right lower quadrant but flatness and, I take it, an increased sense of resistance. That is the most that they could say on physical examination. We do know that he had signs of thrombophlebitis in the left leg. I believe that this patient had a malignant tumor. It may have been retroperitoneal or lower abdominal, and there may have been metastases in the liver. I am sure the decision to explore this case by means of peritoneoscopy was advisable. If cirrhosis was found and nothing else, I do not understand the symptoms.

DR. MALLORY: You see no contraindication to the use of the peritoneoscope in this case, Dr. Jones?

DR. JONES: I think peritoneoscopy should be done. However, the incision should be made as high as possible above the umbilicus because there is the suggestion that something is not right in the lower abdomen and therefore one should keep as far away from this area as possible. My idea in examining this patient would be that one should try to establish two things: first, the presence or absence of liver disease and, second, to see what else there was in the peritoneal cavity. The risk of peritoneoscopy as I see it is minimal and one that has to be accepted to gain further information.

DR. EDWARD B. BENEDICT: Peritoneoscopy showed the abdomen to be so full of adhesions that no air space could be obtained. No implants or tubercles were seen on the adhesions. I could not examine the peritoneal cavity. I tried in two places, just above the umbilicus and then below, and encountered adhesions in both places.

CLINICAL DIAGNOSIS

Carcinoma of liver or peritoneum?

DR. JONES'S DIAGNOSIS

Malignant tumor (abdominal or retroperitoneal).

ANATOMICAL DIAGNOSIS

Tuberculous peritonitis.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Although Dr. Benedict wisely desisted when he encountered adhesions, twenty-four hours following the peritoneoscopy it became obvious that fecal material was draining from the peritoneoscope wound. The patient was therefore taken to the operating room and explored. A generalized adhesive peritonitis was found, and biopsy of the omentum showed that it was tuberculous in nature. An effort was made to seal the point of perforation, which to date has been unsuccessful. The patient still has a draining fistula.

DR. JONES: Was there free fluid in the peritoneal cavity?

DR. MALLORY: No. Is it correct, Dr. Benedict, that we have had other cases of tuberculous peritonitis in which peritoneoscopy has been either difficult or impossible?

DR. BENEDICT: There was one in which I perforated the colon but recognized it right away. The patient was explored immediately, and the opening sutured. But in this case there was no fecal odor, and I know that I was not actually in the bowel. I knew the diagnosis as soon as I found so many adhesions; at least I was reasonably sure that it was tuberculous peritonitis.

DR. MALLORY: The one other type of case that would be equally dangerous would be a diffuse carcinomatous process with adhesions.

DR. BENEDICT: They never give any trouble. I have had a lot of those cases and have never encountered the firm adhesions that you do in tuberculous peritonitis.

DR. MALLORY: So I take it, that if you thought there was a real likelihood of tuberculous peritonitis you would not attempt peritoneoscopy.

DR. BENEDICT: Not if it was the adhesive type.

DR. JONES: I think it is interesting that the x-ray films apparently showed no distortion of the silhouette of the bowel anywhere, or displacement.

DR. MALLORY: After he knew the diagnosis, Dr. Schatzki reviewed the films taken at the time of the small-bowel enema and made this comment:

> Restudy of the films of the small-bowel enema, after being informed about the findings at operation, show that more attention should, perhaps, have been paid several factors. The small intestines filled particularly easily. The loops of the small intestine were grouped in a somewhat too regular order and the tract was, perhaps, slightly shortened. The lower border of the small intestine appeared somewhat smoother and somewhat higher than that usually seen. No intrinsic lesion, however, was present. All these findings together should have made one wonder whether these findings were not consistent with an intraperitoneal chronic disease such as tuberculous peritonitis.

But even after knowing the diagnosis, he did not think that there was anything definite. He believes he might have suspected it.

DR. JONES: I should think one could explain the edema on the basis of malnutrition — that is, nutritional edema. Whether there was ascites at the time it was thought to be present is questionable.

DR. MALLORY: A few months before entry ascites may well have been present. At the time of operation, the peritonitis was the dry adhesive type.

CASE 29062

PRESENTATION OF CASE

A fourteen-year-old girl was admitted to the hospital because of severe abdominal pain.

Two weeks prior to admission, while at camp, the patient suffered with sharp pain in the left lower quadrant, which disappeared spontaneously after two days, without medical care. Approximately four and a half hours prior to admission she was suddenly seized with a similar, but severer, acute, knifelike, intermittent pain in the left lower quadrant involving a 5-cm. area just above and parallel to Poupart's ligament. A short time later the pain radiated to an area above the symphysis pubis. Her physician apparently administered morphine with only slight relief. At times there was a "heavy sensation" in both labia, and slight pain along the medial aspect of the left thigh. There was moderate urgency initially, but this disappeared. The patient had no chills but felt feverish. There was no nausea, vomiting, diarrhea, distention, bloody or cloudy urine or other urinary symptoms.

The family history was noncontributory. The patient was said to have been kicked in the left groin three years previously but suffered only local tenderness, which subsided within a few days. Three months later she was said to have had "catarrhal jaundice," which lasted two weeks. She denied sexual intercourse. Her menses had been normal except that one week before periods there was a slight amount of thick white discharge. The last menstrual period had occurred nineteen days before the present illness. Her cycle was twenty-eight days, and the menses lasted five days.

Physical examination disclosed a well-developed and well-nourished girl who held her left side and cried because of the pain. Examination of the heart and lungs was negative. There was only mild tenderness and spasm in the left lower quadrant, and apparently costovertebral-angle tenderness was not elicited. No masses were felt. There was a slight mucoid vaginal discharge. The introitus admitted two fingers. The cervix was firm and freely movable without associated pain. There was an oblong exquisitely tender mass in the posterior cul-de-sac, which seemed to be a part of the retroverted uterus. It was firm, smooth, movable and about the size of an orange, with a round superior pole that extended up to the left lower quadrant. The ovaries were not felt. Rectal ex-

amination did not contribute any further information.

The blood pressure was 110 systolic, 70 diastolic. The temperature was 100.4°F., the pulse 76, and the respirations 20.

Examination of the blood revealed a white-cell count of 20,500. The urine was normal. A stool was guaiac negative. A cervical smear was negative for gonococcus. A flat plate of the abdomen revealed no unusual soft-tissue masses or areas of calcification.

An operation was performed several hours after admission.

Differential Diagnosis

Dr. Gordon Donaldson: In this case I am afraid the x-ray films are not going to be of much help. I had hoped that the soft-tissue mass might at least be seen, and that we might even be able to see some radio-opaque areas within it. Perhaps Dr. Schulz can outline the mass.

Dr. Milford D. Schulz: Any soft-tissue mass that may be here is indefinite. It would be "sticking one's neck out" to say that such a mass is present.

Dr. Donaldson: With the history of trauma to the left lower quadrant three years previously and with the pain running down along Poupart's ligament with inguinal distribution, I think we must at least mention the possibility of weakness of the abdominal wall or even an actual herniation. However, there was nothing on physical examination to support this suggestion. The urinary tract, too, with this type of radiation might be mentioned as the cause of this girl's pain. A badly prolapsed kidney in the region of this mass would, I should think, have been either atrophic or hydronephrotic by this time and there would have been some urinary findings, which we do not have. The only urinary symptom, moreover, was urgency. I shall also eliminate the gastrointestinal tract, since there was nothing in the history or physical examination to suggest such a lesion.

There is no note in the record of just when her catamenial life began, but I should guess that she had been having periods for a year and a half or two years. This is an ideal time for a hematosalpinx, but to have a large amount of blood in one tube, with the remainder of the genital tract functioning normally and with an undisturbed menstrual cycle, is most unusual.

A tumor of the uterus itself, such as a fibroid, should be mentioned as a possibility. In a young girl who had been menstruating for only a year and a half a fibroid of these dimensions is unlikely.

A tubo-ovarian inflammatory mass should also be considered, particularly since the mass was exquisitely tender. The patient did have a white-cell count that would go with an abscess in that location and she also had a vaginal discharge which was suggestive enough to make someone do a smear. However, there are some inconsistencies with this diagnosis: she was not sick enough, and the temperature and pulse were out of proportion to the white-cell count.

That brings us down to an ovarian tumor, such as a cyst, a fibroma or a dermoid. A tumor of the ovary that had twisted on its pedicle, thus cutting off its blood supply, is an adequate explanation for the elevated white-cell count, the degree of pain and the site of radiation of the pain, although one might have expected that the patient would also have had back pain. The local pressure that such a tumor would exert on the bladder accounts for the urgency and also for the mucoid vaginal discharge. This was probably a dermoid, inasmuch as dermoid is the most prevalent ovarian tumor in a girl of this age; however, I shall not go that far and shall just say that it was an ovarian tumor.

Clinical Diagnosis

Twisted ovarian cyst.

Dr. Donaldson's Diagnosis

Ovarian tumor with twisted pedicle (? dermoid).

Anatomical Diagnosis

Twisted ovarian cyst.

Pathological Discussion

Dr. Tracy B. Mallory: The operation showed that this girl did have a cyst of the ovary. The ovary and tube had twisted on themselves four times, completely infarcting both organs. They were not adherent to surrounding structures, however. The cyst apparently was a simple one, since it contained clear serous fluid. It was not a dermoid. The infarction had completely destroyed its lining cells so that a more exact definition of its character is impossible.

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EPIDEMIC KERATOCONJUNCTIVITIS

An epidemic of keratoconjunctivitis occurred among shipyard workers on the Pacific Coast in 1941.* Since then the disease has gradually spread eastward and has finally appeared in various cities on the eastern seaboard. From an economic standpoint it is of considerable importance, since it disables the worker from two to eight weeks and may seriously interfere with production in any plant where an epidemic takes place.

The etiologic agent is thought to be a virus, particularly since no pathogenic organisms have been recovered from the conjunctival secretions. Scrapings from the conjunctiva show a preponderance of mononuclear cells. The incubation period is from seven to twelve days.

Symptoms consist of a foreign-body sensation in the eye, lacrimation, photophobia, swelling of the lids and enlargement of the preauricular and, sometimes, the submaxillary lymph nodes. There may be slight fever and general malaise. In the early stages the eye shows marked edema of the conjunctiva and the lids. The eye is watery, but there is little or no purulent discharge. After five to ten days there is an involvement of the cornea in from 40 to 60 per cent of the cases. This consists of small subepithelial infiltrates chiefly confined to the central zone of the cornea. The conjunctival symptoms usually subside in from one to three weeks, but the keratitis may remain active for many weeks. As a rule the disease runs a regular course that is little, if at all, influenced by any form of treatment. Since no specific therapy has been worked out, it is better to treat conservatively rather than overzealously. Cold compresses and mild soothing lotions and ointments afford relief, and atropine is indicated if the cornea becomes affected.

Transmission is by direct contact, contaminated hands, instruments, eyedroppers, towels and so forth, and the disease is communicable so long as the conjunctivitis is active. Affected patients should be isolated and should be carefully instructed in eye hygiene. Scrupulous care should be exercised by the physician and his attendants to avoid transfer of the infectious agent: the hands should be washed after examining affected eyes, and instruments and eyedroppers should be sterilized. Although not officially listed as a reportable disease, all suspected cases should be immediately reported to the Division of Communicable Diseases, Massachusetts Department of Public Health, to the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries or to the Division of Industrial Safety, as is brought out in a letter published elsewhere in this issue of the *Journal*.

*Hogan, M. J., and Crawford, J. W. Epidemic keratoconjunctivitis. *War Medicine* 2:984-994, 1942.

MENTAL HYGIENE AND THE WAR EFFORT

The problems of mental hygiene in wartime embrace not only the detection and treatment of mental disease in the armed forces, but the maintenance of services for the mentally deficient among the civilian population in the face of a serious depletion in personnel. That the National Committee for Mental Hygiene and allied agencies are aware of these problems and are prosecuting energetic measures for their solution comes as welcome news to both the medical profession and the public.

First in importance is of course the assurance to the Army and Navy that selectees shall be composed of mentally healthy men. Outstanding progress has been made in this direction in several states, through the co-operation of state departments of mental hygiene and the authorities in Washington. A governmental bureau having agents scattered throughout the country has promised to help in supplying a full-time traveling staff to assist in the supervision of selectees. Men found to be mentally unstable must be protected from the dangers of war duty and be conserved where possible for civilian manpower.

Second only to this necessity is that of detecting and treating cases of mental illness within the armed forces and preventing the development of incipient psychiatric disease. Both the Army and Navy are interested in this program, and have made admirable beginnings in the mental examination of recruits. The National Committee for Mental Hygiene is carrying on a campaign of education among Red Cross workers, medical officers, company commanders, chaplains and others in a position to detect mental cases before they reach the hospital stage. The members of the Military Police have, it appears, been the last to realize their responsibility in this regard, but steps are under way to convert them. A mental-hygiene unit has been established at Fort Monmouth, New Jersey, as an intermediary station between the able-bodied and hospital cases, through the efforts of Brigadier General Edgar L. Crowell, in command of the Signal Corps Replacement Training Center. It is to be expected that similar units will be formed elsewhere, as a part of what the committee considers a momentous development, offering as it does an opportunity never before given for the utilization of social workers in uniform. The American Association of Psychiatric Social Workers has undertaken a year's study of its wartime functions and its resources in personnel, aided by the committee, which is also helping the American Red Cross to solve its personnel problems.

The rehabilitation of mentally disabled civilians and ex-service men is also engaging the attention of the committee. It has established at its headquarters a demonstration rehabilitation unit, to which those rejected by or discharged from the armed forces are referred. In addition, it is pressing for needed federal legislation and striving to show those in authority what an immense source of manpower is represented by the mentally handicapped and those who have recovered from mental illness.

The drastic reduction in civilian psychiatrists and nurses is likely to cause fear on the part of the public that its protection against mental disease will be reduced beyond the point of safety. The committee is meeting this contingency by urging on tardy states a more adequate supervision of mental hospitals and sanatoriums, and by showing mental-hospital authorities that needed attendant personnel can be gathered from the conscientious objectors in civilian service camps; in some cases the wives of such men are employed as attendants, their husbands receiving a small allowance. The committee is also helping child-guidance clinics to secure personnel, and so far no major clinic has been forced to discontinue operation by a shortage of psychiatrists.

In these and many other ways, the National Committee for Mental Hygiene is coping enthusiastically with the mental-hygiene problems of the war. Its efforts are to be commended, and deserve the warm support of the medical profession and the laity.

MEDICAL EPONYM

Stellwag's Sign

"Ueber gewisse Innervationsstörungen bei der Basedow'schen Krankheit [Certain Disturbances of Innervation in Basedow's Disease]" were discussed by Professor Carl Stellwag von Carion (1823–1904), of Vienna, in an article which appeared in the Vienna *Medizinische Jahrbücher* (17: 25–54, 1869). A portion of the translation of his remarks after presenting his theory concerning the disturbances of innervation follows:

> This peculiar pathologic relation is not simply an unrelated, curious finding, but occurs repeatedly in the *disturbances of motility of the lids* which are a constant feature in Basedow's disease. Examples are the abnormal wideness of the palpebral fissure, infrequency and incompleteness of involuntary closure of the lids, and failure of the upper eyelid to participate when the plane of direction of the eyes is elevated or lowered. . . . I have not found this second peculiar phenomenon *(infrequency and incompleteness of involuntary closure of the lids) explicitly* mentioned anywhere in the literature; yet in my observation, it is among the most constant and, indeed, *characteristic* eye symptoms of Basedow's disease.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Analysis of Causes of Maternal Death in Massachusetts during 1941

Miscellaneous (*Concluded*)

During 1941, one death was due to poisoning from diethyl stilbestrol and sulfadiazine. This patient had diabetes. During her pregnancy she had had pyelitis, for which she had been given sulfadiazine; she was also given rather large doses of diethyl stilbestrol. Following her delivery, which was by cesarean section, she had an uncomplicated convalescence until she returned home. Recurrence of the pyelitis was treated by sulfadiazine. Persistent jaundice developed, which resulted in death. Autopsy showed a toxic hepatitis, acute pyelitis and acute nephritis with focal necrosis. This was a tragic disaster.

There was one death due to aneurysm. This patient had had one previous delivery. Her pregnancy had been uneventful until the onset of the fatal illness. The record does not state how far the pregnancy had advanced, but it is reasonable to infer that it was beyond seven months because cesarean section was performed subsequent to laparotomy. The present illness developed suddenly while the patient was mopping the floor. She was said to have had a severe pain in the abdomen and collapsed. She was seen within half an hour and was immediately transferred to a hospital. On entry, the systolic blood pressure was 60, and the pulse 120 and of poor quality. Since the patient presented a picture of extreme shock, immediate laparotomy was decided on. The peritoneal cavity was full of blood, but no definite cause for hemorrhage was found; a cesarean section was performed, there being no statement concerning the condition of the infant. Death occurred twelve hours after operation. An autopsy showed a spontaneous rupture of an aneurysm of the splenic artery. This case illustrates the extreme value of post-mortem examination, without which no specific diagnosis could have been made.

One death was due to hydatidiform mole. This patient was a primipara who was first seen when approximately twelve weeks pregnant, because of bleeding. She was seen in consultation and kept in the hospital 12 days. The diagnosis of threatened miscarriage was made. The bleeding was scanty, and at the end of 12 days the patient was allowed to go home. Three weeks later she began to bleed profusely during the night and was sent to the hospital. On arrival, the pulse was 100. Two hours later a vaginal examination revealed grapelike masses in the vagina. The uterus was curetted, and the vagina was packed. Bleeding was excessive, and the patient died on the operating table. Had a correct diagnosis been made during the patient's first hospital stay and had the uterus been emptied at that time, it is likely that a fatal hemorrhage would not have occurred.

One patient died of psychosis. She was a primipara who was delivered by a cesarean section because of "cervical stenosis." She had lost 20 pounds in the last eight weeks of pregnancy. Following delivery the patient developed a psychosis and would not eat. The psychosis was manic in type, and death resulted from exhaustion and terminal bronchopneumonia, secondary to the psychosis.

One death was due to anaphylaxis. This patient had had eight previous deliveries, all the children being alive and well. She was known to have bronchial asthma, with a particular sensitivity to aspirin. She was delivered normally, and left the hospital seven days later. Two weeks after she had returned home she developed a cold and took some "special cold tablets." An asthmatic attack developed immediately and while being

sent to the hospital in a taxicab, the patient died. This was not a true obstetric death, but since it occurred during the puerperium, it must be so classified.

One patient died of cancer. This patient had three living children. In the fourth pregnancy she was sent to the hospital between the sixth and seventh months, complaining of tenderness in the right lumbar region. There had apparently been no prenatal care. A consultant found a mass in the left breast. At operation on the following day, a scirrhous cancer of the breast was found and the breast was removed. The patient died on the eighth postoperative day; the cause of death was listed as "carcinoma of the breast with carcinomatosis."

Five nonobstetric deaths that were reviewed have not been analyzed.

DEATH

COOK — WILLIAM W. COOK, M.D., of Quincy, died January 23. He was in his fifty-seventh year.

Born in Newcastle, Maine, Dr. Cook received his medical degree from Tufts College Medical School in 1910. He practiced in the Panama Canal Zone for ten years and then in Maracaibo, Venezuela. He was a member of the Massachusetts Medical Society, the American Medical Association and the American College of Surgeons.

His widow, three daughters, a son, a brother and a sister survive him.

CORRESPONDENCE

EPIDEMIC KERATOCONJUNCTIVITIS

To the Editor: A severe and highly contagious form of conjunctivitis, which has been given the name "epidemic keratoconjunctivitis," appeared among shipyard workers in California in September, 1941, and has already appeared in epidemic form in New England. Many doctors have undoubtedly never seen and possibly have never heard of this condition. There are sufficient data to indicate that the disease may easily be transmitted to uninfected persons under treatment for relatively trivial diseases or injuries to the eyes. Three of the four major outbreaks of this disease have occurred in large industrial groups.

The enclosed outline is being sent to physicians and others concerned, to give a clear idea of what to guard against, so that a serious outbreak of a disease which could interfere materially with our total war effort may be prevented.

PAUL J. JAKMAUH, Commissioner of Public Health

JAMES T. MORIARTY, Commissioner of Labor and Industries

A. WILLIAM REGGIO, Surgeon (R), U.S.P.H.S.
Director, Medical Division,
Massachusetts Committee on Public Safety

GEORGE L. SCHADT, President,
Massachusetts Medical Society

EPIDEMIC KERATOCONJUNCTIVITIS

Causative Agent. Presumably a virus.

Incubation Period. Seven to twelve days.

Means of Transmission:

(1) Direct contact.
(2) Contaminated hands, instruments or towels.

Diagnosis:

(1) Edema of one or both lids.
(2) Moderately profuse lacrimation.
(3) Acute follicular conjunctivitis (palpebral and bulbar conjunctivas are both involved).
(4) Early lymph-node involvement, usually with swelling and tenderness of preauricular nodes.
(5) Negative culture.
(6) Development of pseudomembrane in conjunctival sac.
(7) Smear of conjunctival scrapings shows mixed response, with predominance of mononuclear cells.
(8) Development of corneal opacities (a late, not an early, development).
(9) Opacities are small grayish areas below the epithelium, probably located in Bowman's membrane.

Course. In the early stages of the disease, diagnosis is difficult, and the early development of enlargement of the preauricular node should be watched for. The conjunctivitis usually persists ten days or longer, and the corneal opacities generally appear about as the conjunctivitis seems to be disappearing. The usual therapeutic agents are of little or no use, and no specific therapy is yet available. About 50 per cent of the cases develop bilateral involvement. The disease has been known to persist as long as eight weeks. In one epidemic, 85 per cent of the patients developed corneal opacities, and these appear to be permanent in the majority of cases.

Treatment. There is no specific therapy. Sulfonamide ointments and solutions have been used extensively. Cold compresses seem to produce more relief from discomfort than hot.

Recommendations:

(1) Meticulous cleansing of hands and instruments by physicians, nurses and so forth.
(2) Use individual eyedroppers.
(3) Establish early diagnosis.
(4) Isolation of infected patients.
(5) Education of patients in measures of general cleanliness and eye hygiene.

Outbreaks of this disease, real or suspected, should be reported immediately to one of the three following agencies, from which further information may be obtained:

Division of Communicable Diseases
Department of Public Health
519 State House, Boston (CAP 4600)

Division of Occupational Hygiene
Department of Labor and Industries
23 Joy Street, Boston (CAP 0687)

Division of Industrial Safety
473 State House, Boston (CAP 4600)

Research in the epidemiologic and bacteriologic aspects of the disease is being carried on under the direction of Dr. Murray Sanders, Columbia University College of Physicians and Surgeons, 630 West 168th Street, New York City.

HAND–SCHÜLLER–CHRISTIAN DISEASE

To the Editor: I regretted to see in the November 12 issue of the *Journal*, which I peruse regularly, that the eponym for the week ["Schüller–Christian"] left out the name "Hand" from the condition that he was the first to describe. In fact I have always thought that Schüller added less than either Henry Christian or Dr. Hand (who, by the way, is still practicing in Philadelphia), although together they did not give an adequate nosologic picture. Certainly Hand's description appeals to me as nearer the mark than Schüller's conclusions that are translated.

E. B. KRUMBHAAR, M.D.

The School of Medicine
University of Pennsylvania
Philadelphia

* * *

Dr. Krumbhaar's letter was referred to Dr. Robert W. Buck, the author of the eponyms; his reply was as follows:

To the Editor: I read with interest Dr. Krumbhaar's letter concerning Hand–Schüller–Christian disease. My original typescript regarding Schüller–Christian disease must have been written nearly ten years ago, at which time I knew nothing of the xanthomatoses. As Dr. Krumbhaar points out, Hand was as nearly correct as either Schüller or Christian. I think the proper eponym at the present time is "Hand–Schüller–Christian," and I should include the descriptions of all three authors.

ROBERT W. BUCK, M.D.

5 Bay State Road
Boston

REPORT OF MEETING

HARVEY SOCIETY

At a regular meeting of the Harvey Society of Tufts College Medical School, held at the Beth Israel Hospital on October 23, Dr. Harold W. Brown, dean of the School of Public Health of the University of North Carolina, spoke on the subject "Intestinal Anthelmintics." Formerly, the treatment of helminthiasis was based on erroneous reasoning, being aimed at disgusting the parasites with foul-smelling, foul-tasting medicines. Fortunately for the far-flung armed forces of the United Nations in the present world conflict, who are stationed in areas infested with these parasites, knowledge is now based on scientific facts; however, it is still incomplete, so that some methods of treatment are empirical.

The chief characteristics of the group of worms that infest the intestinal tract are as follows: they usually have a digestive tract; most of them have a low-grade nervous system; they have no heart; there is a rudimentary excretory system; and they have a horny outer layer of chitin that is like the substance forming a fingernail. It becomes obvious, therefore, that anything which affects such an organism must also be toxic to some extent on the host. Furthermore, these intestinal helminths vary in habits, anatomy, size and position, so that "shotgun therapy" is of no avail. For example, the hookworm is small and cannot be affected until the bowel is cleaned, whereas the ascaris is large and is not easily protected by food. This is one of the reasons for the rationale of purges. Further reasons for the employment of purges are to rid the host of toxins and to wash out worms that may only have been stunned by the anthelmintic.

Anyone concerned with the therapy of helminthiasis should be able first to diagnose the kind of worm responsible. This requires a fundamental knowledge of the various kinds of eggs.

The hookworm is a parasite about 1.0 cm. long that has teeth which fasten onto the wall of the intestinal tract of the host; therefore the aim of treatment is to break this grip. Chloroform was once used; this drug does stun the worm, but it is liable to injure the liver of the host. One part of chloroform is soluble in 200 parts of water; hence, much is probably absorbed from the intestinal tract. In an effort to find a solution of lower solubility and toxicity, carbon tetrachloride was employed. Since 1 part of this is soluble only in 2000 parts of water, there is less absorption from the intestinal tract of the host. A subsequent purge rids the alimentary tract of the stunned worms and further decreases the chance of toxic effects. However, this drug was found to have fatal results once in 30,000 to 50,000 cases, and even such a low mortality cannot be countenanced in public-health work, where the good will of the community is needed. This led to further research and to the discovery of the efficacy and nontoxicity of tetrachlorethylene. Since the solubility of this drug is only 1 part in 12,000, intestinal absorption is practically negligible. Furthermore, this compound is available and relatively cheap. The dose is 3 cc. Giddiness is an occasional complaint, and rare cases of coma occur. Alcohol increases the rate of absorption and therefore adds to the danger of toxic reactions.

Although carbon tetrachloride has been supplanted in the treatment of hookworm disease, it is still the treatment of choice in tapeworm infestation. Injury to the liver apparently occurs only in the presence of low calcium and carbohydrate reserves. In suspected cases of deficiency, therefore, the patient should be given a high-milk, high-carbohydrate diet for some time before the anthelmintic is employed. These parasites grow from the head, and therapy is aimed at this part of the organism. The weight of the rest of the worm, which often is 15 to 20 feet long, aids in freeing the head by gravity, even if the worm is only stunned. If the body and not the head is obtained, there is no advantage in attempting treatment again for about two months, since it is rare that the head can be dislodged without the beneficial effect of the weight of the body.

A combined infestation with round worms (Ascaris) and hookworms is not infrequent, and its management entails some difficulties. Both carbon tetrachloride and tetrachlorethylene stimulate the former, and, in an attempt to escape, they are liable to enter the biliary tract or peritoneal cavity. Careful diagnosis obviates this danger. Oil of chenopodium, of which ascaridole is the active principle, is effective against this worm, but is of relatively high toxicity, death occurring about once in every 20,000 to 40,000 cases. There is often a question of idiosyncrasy to the drug. Experiments were carried out with the phenol and resorcinol derivatives in an attempt to find a compound that would be effective and at the same time nontoxic. Increasing the side chain decreased the toxicity to both worms and man, and it was found that the most potent anthelmintic for this species that was relatively safe for man was hexylresorcinol. This kills 95 per cent of the worms and cures 90 per cent of patients. The dose is 1 gm. This drug precipitates protein and

forms a close bond with it, so food should not be given for five hours before or after treatment. Because of this property of protein precipitation, hexylresorcinol may affect the mucous membrane of the buccal cavity if taken by mouth in its native state. Gelatin capsules are usually used, but these are difficult for children to swallow.

Whip-worm (Trichuris) is not effectively combated by any single drug, although any of the usual anthelmintics kill a few. *Leche de higneron* (milk of the fig tree) is said to have been used successfully in Venezuela, but this is a particularly foul-tasting substance, of which a dose of 60 cc. is required. Its action is supposed to be due to fecin, a specific enzyme, which kills the worm by digestion. This enzyme has not been isolated.

BOOK REVIEWS

Principles of Extraperitoneal Caesarean Section. By James V. Ricci, M.D. 8°, cloth, 224 pp., with 47 illustrations. Philadelphia: The Blakiston Company, 1942. $4.50.

This monograph, divided into eleven chapters, deals exclusively with the various modalities of the lower-segment cesarean sections.

In the first chapter, entitled "Gastro-Elytrotomy," the authors discuss the principles of extraperitoneal cesarean section and show, by an extensive review of literature, the various steps in the evolution of this operation. In the second chapter, which covers the period from 1906 to 1940, the intra-abdominal lower segment, exclusion and extraperitoneal types of cesarean section are elaborated. The appended bibliography, because of its completeness, is in itself a definite contribution to this subject. In the third chapter, the anatomy and histology of the isthmus and the lower segment, so necessary for a clear understanding of extraperitoneal approach in cesarean section, are lucidly described. The authors contend that the fully developed lower uterine segment originates from both the isthmus and the portio abdominalis of the cervix. The anatomy and histology of the fascia and its relation to the bladder, the lower segment and the peritoneum form the subject matter of the fourth chapter. This is well illustrated by means of line drawings and photomicrographs, and helps to visualize what takes place when these structures are separated from each other during the performance of extraperitoneal cesarean section. Chapter five covers incisions, scars and ruptures of the lower segment. Two types of incisions may be placed in the lower segment, the transverse incision and the longitudinal incision, both of which are discussed, their favorable and unfavorable points being brought out. The authors, who favor the transverse incision state, "In America, despite Phaneuf's contribution, DeLee's persistent advocacy of the longitudinal incision has retarded the adoption of the transverse lower segment incision." They show that Waters and Ricci have adopted the transverse incision in the true extraperitoneal cesarean section. Ruptures of the lower segment in subsequent pregnancies and labors are considered in detail. It is shown that most of the reported ruptures of lower-segment incisions followed longitudinal incisions. The methods of delivery in extraperitoneal cesarean section are treated in the sixth chapter, whereas in the seventh, wound infections and methods of drainage are elaborated. The authors advocate, whenever feasible, draining per vaginam. In the eighth chapter the technics of the extraperitoneal types of cesarean section are explained, and a concise table summarizing the various extraperitoneal technics adds to the value of the presentation. All methods of extraperitoneal approach are commented on, and four stand out: those of Latzko and Küstner, both with longitudinal incisions in the lower uterine segment, and those of Waters and Ricci, where the lower segment is incised transversely — the second Latzko operation in America is said to have been performed by James W. Markoe of the New York Lying-In Hospital. Because of the better exposure obtained the operations of Waters and Ricci are consistently gaining in favor in America and are supplanting those of Latzko and Küstner. The procedures of Waters and Ricci are well illustrated; they differ mainly in the method of the separation of the intact peritoneal sac from the bladder in exposing the lower segment. Chapter nine explains the essential factors in the execution of the Physick–Sellheim extraperitoneal cesarean section and is a recapitulation of the technical details elaborated in the previous chapters. The tenth chapter stresses extraperitoneal cesarean in patients previously cesareanized or laparotomized. By means of well-adapted illustrations, the authors show how the difficulty of adhesions may be overcome and how an extraperitoneal cesarean section may be repeated should the occasion arise. Finally, in the eleventh chapter, the operative and postoperative complications, which consist of injuries to the peritoneum and bladder during the dissection, are discussed in detail, and methods for the repair of these injuries are given. Fundal packing and hemorrhage are touched on, as are hematomas and retrovesical phlegmons.

The illustrations throughout this book are carefully chosen and well executed, and one is impressed with the tremendous amount of work required in the extensive compilation of the literature of lower-segment cesarean section. This monograph should prove to be of value to the obstetric specialist and should serve as ready reference for writers on the subject; whereas from a historical standpoint, it should interest all physicians who practice obstetrics.

The Management of Fractures, Dislocations and Sprains. By John A. Key, M.D., and H. Earle Conwell, M.D. Third edition. 4°, cloth, 1303 pp., with 1259 illustrations. St. Louis: The C. V. Mosby Company, 1942. $12.50.

The appearance of the third edition of Key and Conwell's treatise on fractures and sprains marks an endeavor to produce an up-to-the-minute discussion of subjects than which there are scarcely any of greater importance. New methods are being introduced so rapidly that it is difficult to evaluate their comparative efficiency. Good results are obtained by old and outmoded methods. The important fact to remember is that each case is a law unto itself. There will inevitably be differences of opinion concerning the merits of different technics but, among them all, there will probably be at least one that may be applied to the condition in hand.

The methods set forth in this book are advocated by two authors whose opportunities for studying a large number of fractures and sprains have been extensive, and their opinions cannot be lightly brushed aside. For those who can hospitalize their cases of fracture, where it is possible to take advantage of all the modern facilities for dealing with these conditions, this volume should be of considerable value, since it outlines the authors' experiences in handling a large number of such lesions. One should remember, however, that facility in the employment of modern technics is the key to their satisfactory use. As a reference book for the guidance of such individuals this volume has much to recommend it, although in the management of some types of fracture

there will be divergences of opinion regarding the propriety of certain of the suggestions offered.

It is unfortunate that the book is so bulky and heavy, which interferes with its convenient use.

Administrative Medicine. Edited by Haven Emerson, M.D. 4°, cloth, 839 pp., with 39 figures, 82 tables and 18 charts. New York: Thomas Nelson and Sons, 1941. $7.50.

This book should convince the most skeptical that administrative medicine is worthy of being considered a medical specialty or specialties. Dr. Emerson's long association with practically all types of medical, medico-social and public-health activities has enabled him to develop a comprehensive collection of subjects and to select writers who were not only familiar with their subjects but also forward-looking and future-minded.

The same general plan is followed in presenting each subject. First, a short historical sketch of its development; next, a consideration of the present organization and activities, with indications of the trends; and then, in some cases, definite suggestions concerning future developments.

The book is divided into three parts. Part I deals with the organized care of the sick, hospitals of all kinds, convalescent homes, outpatient service, home care, visiting nurse service and, finally, the latest development, voluntary hospital-care insurance. Each author is a master of his subject. Part II discusses public-health services. International, national, state and local public-health organizations are clearly delineated. Then follows a series of interesting chapters on what might be termed the public-health specialties — vital statistics, communicable-disease control, occupational hygiene, milk control and laboratories, to mention only a few. Persons who believe themselves well informed will learn much by reading these chapters. Part III covers "inclusive medical care" for prevention and treatment. The description of the medical services of the armed forces is particularly complete and clearly set forth, but under the stress of war probably is now undergoing marked changes.

The chapters "Medical Services under Government Auspices in the United States and Canada" and "Economic and Social Aspects of Administrative Medicine" are complementary, the first setting forth the present stage of development of governmental participation and the latter presenting the arguments for future developments along the line of compulsory health legislation.

This book should be most useful as an authoritative, up-to-date encyclopedia on the subjects presented.

The Modern Attack on Tuberculosis. By Henry D. Chadwick, M.D., and Alton S. Pope, M.D. 8°, cloth, 95 pp., with 5 illustrations and 8 tables. New York: The Commonwealth Fund, 1942. $1.00.

With the steady decline in the morbidity as well as the mortality from tuberculosis the time has come when the final attack for its complete eradication must be planned with vigor and determination. It is with this thought in mind that this book has been written. The authors state in their preface that they make no pretense of adding to the sum total of knowledge concerning tuberculosis. They believe that sufficient facts are already available to make the eradication of tuberculosis a possibility within a few generations if the established technics are effectively applied. The writers are men of many years of experience both in the clinical as well as in the public-health field and thus can speak with authority and mature judgment.

The worthwhileness of this book is enhanced by its clarity and brevity. This small book, divided into six chapters, is cramped with information and important facts regarding the final triumph over the age-old scourge of tuberculosis. The authors' emphasis is centered on the prompt discovery of tuberculous infection and the early segregation and treatment of cases. Case finding in the community is the modern watchword of the health worker. Although early diagnosis was the goal of the tuberculosis worker twenty-five years ago, his modern counterpart goes out into the field and searches for latent foci of infection in the most susceptible portion of the community. Thus the authors urge mass x-ray examinations of students, — especially embryo physicians and nurses, — patients in prenatal clinics, all contacts and elderly persons. They also stress the sanatorium as not only the place for the treatment but also the place for the segregation of infected persons. Thus they plead for more sanatorium beds in more attractive surroundings with greater appeal to patients. The authors dare to prophesy that the bells that ring in 2000 may sound the death knell of the tubercle bacillus.

The scientific and the public-health aspects concerning the eradication of tuberculosis are clearly and authoritatively covered in this book. It should serve as a useful guide not only to tuberculosis workers but also to all interested in community health.

Internal Medicine in Old Age. By Albert Mueller-Deham, M.D., and S. Milton Rabson, M.D. 8°, cloth, 396 pp., with 10 illustrations. Baltimore: The Williams and Wilkins Company, 1942. $5.00.

The authors of this book, after a brief discussion of certain general aspects of old age, present "internal diseases," system by system, as they occur in the aged. In consequence of this chosen limitation, two important features of practice among the old — psychologic problems and problems on the border line between medicine and surgery — are omitted. In the present state of knowledge of geriatrics, the field should be covered for the practitioner relatively simply. Authors of books of this sort, however, err in including too many individual diseases, concerning certain of which there is nothing of consequence to be said. For example, in this book there are discussions of scurvy, agranulocytosis, amebic dysentery and Weil's disease that will not help the physician who deals with the aged as much as those in any standard textbook of medicine. Moreover, in this book the authors often recommend treatment that is unacceptable to many physicians in this country: "transpulmin" in pneumonia; creosote, guaiacol and tuberculin in tuberculosis; iodides in arteriosclerosis; neoarsphenamine in "coccal or mixed infections" of the bladder; "interdiction of meat" and limitation of other proteins in impending hepatic failure and so forth. There is much insistence on the weight of individual experience in rendering judgment on the efficacy of treatment, a form of argument that is least convincing to the critical mind. Physiologic mechanisms, such as those of angina pectoris and hypertension, are described, but with serious inadequacy. On the other hand, anatomic changes are more richly and more satisfactorily presented than in other available books in this field. It is only for this feature that the book can be recommended.

Immunity against Animal Parasites. By James T. Culbertson, B.S., A.M., Ph.D. 8°, cloth, 274 pp. New York: Columbia University Press, 1941. $3.50.

This monograph by a member of the Department of Bacteriology of Columbia University satisfactorily replaces the second edition of *The Immunology of Parasitic Injections*, published in 1929 by another expert in the field of animal parasitology.

It is divided into three parts. The second part, which deals with immunity in specific diseases, makes up the bulk of this book. With Taliaferro's classic textbook as its point of departure and citing almost all the significant papers issued after 1929, it gives thorough information on natural and acquired immunity against animal parasites.

The third part, consisting of only three of the twenty chapters, will be welcomed by the general practitioner who wants a review of vaccinations and diagnostic tests that are of recognized value.

The first part, although presupposing a knowledge of microbiology, is highly useful for it gives a general introduction to and the fundamental principles of the subject. With a few exceptions, for instance, the form of resistance called "premunition," studies on the mechanisms involved in immunity against animal parasites follow a path that is identical with the one opened up by investigations concerning immunity against pathogenic bacteria. Even ablastic antibodies, which have been demonstrated by Taliaferro in immune serums against trypanosomes and by Campbell in immune serums against cestodes, trace their origin to antibodies uncovered in immune serums against anthrax and swine erysipelas. They have also been called "azygots" in order to point out their lack of absorption by homologous antigens. Culbertson, although conceding that ablastic antibodies are not absorbable, maintains that their effect is due to their union with the antigens of the parasites. Considering the effort required to gather the heterogenous literature on this matter, such a logical incompatibility and a few other discrepancies are quite understandable and do not affect the usefulness of this able attempt to give thorough orientation in a specialized branch that had to be worked out in a form accessible to the student, as well as to the practicing physician or veterinarian.

The illustrations, charts and tables have been selected with a didactic flair that will be appreciated particularly by the teachers, who henceforth will have at hand a treatise that they can resort to when lecturing on immunity against animal parasites.

The Principles of Anatomy: As seen in the hand. By Frederic Wood Jones, D.Sc. (Lond., Adelaide and Melbourne), F.R.S., F.R.C.S. Second edition. 8°, cloth, 418 pp., with 144 illustrations. Baltimore: The Williams and Wilkins Company, 1942. $7.50.

The first edition of this well-known work, published in 1920, was prepared during World War I as part of the course of instruction to officers of the Royal Army Medical Corps to qualify them to care properly for military injuries of the hands. This second edition, similarly a product of war, is brought to date by the addition of six new chapters and twenty new figures in the text.

The author emphasizes topographical and functional anatomy, and uses the hand as an example of an anatomical method that can be applied to other regions. Beginning with phylogenetic and morphologic considerations of pentadactylism and polydactylism, he discusses the comparative digital, phalangeal, metacarpal and carpal formulas of man and of other animals. Similarly he deals with flexure and cleavage lines, papillary ridges, nails, functions, fascias, bones, joints and sesamoids of the hand. In his study of morphology of the extrinsic and intrinsic musculature, he quotes Dwight's cautioning stricture that "to find in man an occasional form of a muscle that is normal in no matter what animal" does not necessarily explain "how the peculiarity could have been transmitted." Finally he gives in detail not only the vascular and lymphatic channels and arteriovenous anastomoses of the hand but also its somatic and autonomic nerves and the sensory and motor pathways that connect it with the brain. His method is illuminating, his observation accurate, his descriptions detailed, his interpretations conservative. Particularly valuable are his analyses of "trick movements" following nerve injuries.

As a text of applied anatomy, combined with such a clinical work as that of Kanavel, this book is of timely value to military surgeons preparing to treat war injuries of the hands. It is provided with many admirable illustrations and with well-selected references for further reading.

Castor Oil and Quinine: Once a doctor, always a doctor. By George W. Vandegrift, M.D. 8°, cloth, 252 pp. New York: E. P. Dutton and Company, Incorporated, 1942. $3.00.

This is the biography of a New York physician who practiced from 1879 onward on the lower East Side of the city. The story is written by his son, presumably from authentic evidence received from his father. The elder Vandegrift was a typical "corner doctor." He soon established himself at the junction of two well-known streets, and treated everybody who came to his door for any sort of an illness. It was a rough sort of practice, but the art of medicine has seldom been better exemplified than in the story of this untutored, honest practitioner. The book gives the story of medicine as practiced in a big city and in a ward filled with Irish and German immigrants during the latter quarter of the nineteenth century. Vandegrift's account of his father is interesting and readable, and in many ways may be considered a unique document. The title gives the clue to the type of medicine practiced by this pioneer physician, for he, indeed, was as much of a pioneer as the man who went into the Far West during the early days of the century.

The Care of the Aged: Geriatrics. By Malford W. Thewlis, M.D. Fourth edition, thoroughly revised. 8°, cloth, 589 pp., with 50 illustrations. St. Louis: The C. V. Mosby Company, 1942. $7.00.

In this edition, as in its predecessors, the author gives some consideration to the practical handling of most of the medical problems of old age. Unfortunately, knowledge of the fundamental characteristics of the aged, which must determine special aspects of their treatment, is fragmentary. As the title indicates, a summary of even this incomplete knowledge is outside the scope of the book. Hence, the uncertainties of geriatrics and the fundamental problems that await clarification and solution receive little emphasis. Furthermore, the book seems to slight the psychologic aspects of disease and treatment in old age. Since the author undertakes to deal with a wide range of diseases, it is to be expected that specialists will disagree with his advice in not a few instances. Nevertheless, the practitioner will find this the most helpful book in the field.

NOTICES

MASSACHUSETTS GENERAL HOSPITAL

A meeting of the Hospital Research Council will be held in the Bigelow Amphitheater of the White Building on Tuesday, February 23, at 5 p.m.

PROGRAM

The Effect of Cholesterol Administration on Anesthesia. Drs. F. F. Foldes and H. K. Beecher.

Ocular Maldevelopment in Premature Infants. Dr. T. L. Terry.

Study of Some Growth Factors Associated with Oral Aciduric Bacteria. Dr. D. Weisberger.

The Action of Soap on the Skin. Drs. C. G. Lane and I. H. Blank.

CARNEY HOSPITAL

The monthly clinical meeting and luncheon of the Carney Hospital will be held in the hospital auditorium on Monday, February 15, at 11:30 a.m. Following routine business, case reports will be presented.

Physicians and medical students are invited to attend.

WASHINGTONIAN HOSPITAL

A round-table discussion of "The Sociological Aspects of Alcoholism" will be held at the Washingtonian Hospital, 41 Waltham Street, Boston, on Sunday, February 14, at 5:00 p.m.

All interested persons are cordially invited to attend.

BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held in the Amphitheater of the White Building, Massachusetts General Hospital, on Wednesday, February 17, at 8 p.m.

PROGRAM

Sensitivity to High Tensions of Oxygen. Drs. C. M. Williams and H. K. Beecher.

Chemical Compounds Inhibiting the Action of the Thyroid Gland. Dr. E. B. Astwood.

Certain Aspects of the Role of the Adrenal Cortex in Anoxia. Dr. M. Clinton, Jr.

NEW ENGLAND ROENTGEN RAY SOCIETY

A meeting of the New England Roentgen Ray Society will be held in the Bartlett Room of the Harvard Club on Friday, February 19, from 4:30 to 6:00 p.m. There will be an x-ray conference, and all are requested to bring cases proved by operation, biopsy or autopsy. At 6:00 p.m., dinner will be served, after which the following program will be presented:

8:00 p.m. An Unusual Cause of Small-Bowel Dilatation. Dr. Clayton Hale.

8:10 p.m. A Mediastinal Mass of Unusual Etiology. Dr. Morton Mazer.

8:20 p.m. Symposium on Bronchiogenic Cysts: Embryology and Pathologic Anatomy, Dr. Tracy B. Mallory; The Radiological Appearance, Dr. Laurence Robbins; Surgical Consideration, Dr. Richard Sweet.

(Notices continued on page x)

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SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, February 14

Sunday, February 14

*3:00 p.m. Early Treatment of Traumatic Injuries of the Face and Jaw. Dr. V. H. Kazanjian. Symposium on Aviation Medicine. Cheever Amphitheater, Dowling Building, Boston City Hospital.

†4:00 p.m. Problems of Ventilation in the Home. Dr. Constantin P. Yaglou. Amphitheater of the Peter Bent Brigham Hospital.

*5:00 p.m. The Sociological Aspects of Alcoholism. Round-table discussion. Washingtonian Hospital, 41 Waltham Street, Boston.

Monday, February 15

*11:30 a.m. Carney Hospital. Monthly clinical meeting and luncheon.

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, February 16

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. The Use of the Sulfonamide Drugs in Medical Practice. Dr. Charles A. Janeway. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

8:00 p.m. New England Ophthalmological Society. Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston.

Wednesday, February 17

*9:00–10:00 a.m. Bacterial Allergy. Dr. Ethan Allan Brown. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

8:00 p.m. Boston Society of Biologists. Massachusetts General Hospital, amphitheater of the White Building.

Thursday, February 18

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

Friday, February 19

*9:00–10:00 a.m. The Sulfonamides. Dr. C. A. Janeway. Joseph H. Pratt Diagnostic Hospital.

4:30 p.m. New England Roentgen Ray Society. Harvard Club, Boston.

Saturday, February 20

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

*Open to the medical profession.

†Open to the public.

February 13. American Board of Obstetrics and Gynecology. Page 690, issue of October 29.

February 23. Massachusetts General Hospital. Hospital Research Council. Page ix.

May 25 and 26. Massachusetts Medical Society. Hotel Statler, Boston.

District Societies

BRISTOL SOUTH

May 6. New Bedford.

ESSEX NORTH

May 5.

ESSEX SOUTH

March 3. Essex Sanatorium.

April 7. Addison Gilbert Hospital, Gloucester.

May 5. Salem Country Club.

FRANKLIN

March 9.

May 11. Annual meeting.

Meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE

March 3.

May 5.

MIDDLESEX EAST

March 17. Bear Hill Golf Club, Stoneham, 12:15 p.m.

May 5. Bear Hill Golf Club, Stoneham, 6:30 p.m.

(Notices continued on page xiii)

MIDDLESEX NORTH
April 28.
July 28.

PLYMOUTH
February 18. Jordan Hospital, Plymouth.
March 18. Goddard Hospital.
April 15. Bridgewater State Farm.
May 20. Lakeville.

WORCESTER
March 10. Memorial Hospital, Worcester.
April 14. Hahnemann Hospital, Worcester.
May 12. Annual meeting.

WORCESTER NORTH
April 28.
July 28.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Aftereffects of Brain Injuries in War: Their evaluation and treatment, and the application of psychologic methods in the clinic. By Kurt Goldstein, M.D., clinical professor of neurology, Tufts College Medical School. With a foreword by D. Denny-Brown, M.D., professor of neurology, Harvard Medical School and head of the Neurological Unit, Boston City Hospital. 8°, cloth, 244 pp., with 46 illustrations and 2 plates. New York: Grune and Stratton, 1942. $4.00.

This work is written for the specialist who has to deal with injuries of the nervous system. It is divided into two parts, the first having to do with symptomatology and the second with treatment of various conditions amenable to physical and neurologic therapy.

Practical Survey of Chemistry and Metabolism of the Skin. By Morris Markowitz, M.D., associate in dermatology and syphilology, Graduate School of Medicine, University of Pennsylvania, and dermatologist to St. Luke's and Children's Medical Center and St. Christopher's Hospital, Philadelphia. 8°, cloth, 196 pp. Philadelphia: The Blakiston Company, 1942. $3.50.

This small manual is intended to furnish fundamental facts necessary for a better understanding of dermatology. In addition to chemistry and metabolism, there is also included blood chemistry and a description of vitamins and vitaminoses as related to skin diseases.

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